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CHARCOT'S JOINTS[1]

By CHARLES G. SUTHERLAND, M.B. (Tor.)
Section on Roentgenology, Mayo Clinic, ROCHESTER, MINNESOTA

IN A series of lectures delivered at La Salpetrière, Charcot, Professor of the Faculty of Medicine of Paris, discussed the arthropathies of cerebral or spinal origin. He divided these into two types: (1) subacute or acute arthropathies, accompanied by tumefaction, redness, and sometimes by pain, associated with traumatic or inflammatory lesions of the cord, and (2) those associated with locomotor ataxia. Cases of the first type were first reported by an American physician, Mitchell (1831), who observed it in the paraplegia connected with Pott's disease. Allison, in 1846, and afterwards Brown-Séquard, described the arthropathies of paraplegic patients. These conditions were limited to the paralyzed limbs and, because of the anatomic and clinical characteristics cited, were placed by Charcot in the category with those he described in 1862. As nowhere in the voluminous literature on this subject have I found a more concise or comprehensive description of this lesion than that of Charcot's original article, I consider it worth while to quote from his lecture.

"The disorder generally shows itself at a determinate epoch of the ataxia, its appearance coincides in many cases with the setting in of the motor inco-ordination. Without any appreciable cause, we may see, between one day and the next, the development of a general and often enormous tumefaction of the member, most commonly without any pain whatever or any febrile reaction. At the end of a few days the general tumefaction disappears, but a more or less considerable swelling of the joint remains, owing to the formation of hydrarthus; and sometimes to the accumulation of liquid in the periarticular serous bursa also. On puncture being made, a transparent, lemon-colored liquid has frequently been drawn from the joint. One or two weeks after the invasion, sometimes much sooner, the existence of more or less creaking sounds may be noted, betraying the alteration of the articular surfaces, which, at this period, is already profound. The hydrarthus becomes quickly resolved, leaving after it an extreme mobility of the joint. Hence consecutive luxations are frequently found, their production being largely aided by the wearing away of the heads of the bones which has taken place. I have several times observed a rapid wasting of the muscular masses of the members affected by the articular disorder. One anatomo-pathological character is apparently constant, namely, the enormous wearing down of the articular surfaces of the extremities in a very short time. Besides the wearing down of the articular surfaces you notice here the presence of foreign bodies, of bony stalactites, and all the customary accompaniments of arthritis deformans. These latter alterations * * * are produced in an accidental manner,

[1] Read before the Radiological Society of North America, at Kansas City, December, 1924.

chiefly by the movements to which the patients subject the affected members. The articular affection in question is, itself also, the expression of trophic disorders directly dependent on the lesion of the spinal nerve center."

In the analysis of 246 cases of arthropathy, Henderson found that 54 of the patients were in the pre-ataxic stage, 36 in the transitional stage, and in 156 the ataxia was well marked. In his experience, about 5 per cent of ataxic patients had Charcot's joints. Carman found the incidence to vary from 1.75 per cent in Limbach's tabulation of Erb's 400 cases, to Bramwell's 6 per cent of a total of 270 cases. The tabulations of several observers indicated that the disorders were more common in the lower extremities, the knee, hip, ankle, and foot being affected in the order named, and the shoulder less often.

Similar arthropathies were seen as a complication of syringomyelia, in which, in contrast to locomotor ataxia, the distribution was more common in the upper extremities, the shoulder, elbow, wrist, hip, knee and foot being affected in the order named. In reporting three cases of arthropathy complicating syringomyelia, two in the shoulder and one in the elbow, Koopmans warned that in cases of arthritis deformans, particularly in the young, syringomyelia should be kept in mind; it is more likely to be present when there is a destructive process or a dislocation within or near the joint. He believed that recurring dislocation of the shoulder was frequently due to syringomyelia.

A complete disorganization of the wrist joint was noted by Duncan to have occurred four years after a severe injury to the brachial plexus by a falling log. Phillips described an interesting case of arthropathy in the shoulder; the patient was an ice man and the arthropathy followed long-continued strain from pulling on heavy blocks of ice and carrying these on the shoulder.

Syringomyelia was found at necropsy in a patient with Paget's disease, and Marie advanced theories to explain this by mechanical factors.

Arthropathies similar to, or identical with, those observed in tabes dorsalis, were reported as associated with general paralysis of the insane, by Stern; as complicating psoriasis, by Adrian; leprosy, by Waelsch; and anterior poliomyelitis, compression and destruction of the spinal cord, or following severance of nerves, by Adami. Dercum described trophic changes, occurring in a tabetic person, suggesting acromegaly. Carman, in a review of the literature, found among the complications that might interfere with a clinical diagnosis two reports of suppurative arthropathy in tabetic persons, and an ultimate tuberculization of a tabetic arthropathy.

Charcot made the first report of a spinal arthropathy in 1874, with an excellent drawing of the spine. Jones found thirty-two cases in the literature, including Charcot's, and added two of his own. Ridlon, reporting ten cases, commented on the findings of previous writers, who had localized the majority of lesions in the cervical region; one observer doubted whether it ever occurred in the dorsal or lumbar vertebræ. In Ridlon's cases the lesions all involved the lumbar vertebræ. He believed that the spine was not often involved in the secondary stage; the greater number of bone changes, in his experience, originated in the tertiary stage. Roger, in 1923, found reports of sixty cases of spinal arthropathy in the literature and added seven cases of his own. One of Roger's patients, a morphine habitué, had increased fragility of the bone and multiple fractures, similar to that seen in cases of osteomalacia.

An interesting experiment was carried out by Eloesser, who presented his findings in 1917. He selected three problems: (1) Are tabetic arthropathies due purely to degeneration of certain nerves that cause the bone to atrophy (Charcot's theory)? (2) Are they simply syphilitic arthritides, occurring sometimes in the course of tabes, but not infrequently in the absence of any

lesion of the nerve (Barrie and Bainski)? (3) Are they due to the combined influence of lesions of the nerve and bone? Cutting the posterior roots that lead to a particular extremity, in cats, enough to make a total analgesia, anesthesia and ataxia, Eloesser produced an ascending degeneration of the posterior columns corresponding to what would be in man a one-sided tabes. Some of these animals developed Charcot's joints or tabic fractures. He then produced joint changes, and, after waiting some time, cut the posterior roots and found that the course of a deforming arthritis was not characteristically altered by the addition of an analgesic factor. The cutting of three dorsal roots leading to as many ribs did not result in atrophy of the bone, and the study of bones from the extremities corroborated this finding. He resected the posterior roots in three cats, and, after waiting a number of weeks, opened the joints, seared a spot on the femoral condyles with a thermocautery, and produced, within three weeks, typical Charcot's joints in all animals. Of thirty-eight animals with disturbances of the sensibilities of the legs, twenty-seven developed spontaneous lesions of bones and joints; eight of these joints, showing the periarticular ossifications and destructive arthritis typical of Charcot's joints, were the seats of fractures that ran into or near the joint. Trauma and the lack of the warning sense of pain, in his opinion, were the cause of most tabic bone and joint lesions. In another contribution (8), he called attention to the tabes occasionally associated with acute Charcot's joint, usually the result of trauma, and pain in and around the joint. Eloesser's experimental work led him to believe that the skin might retain the sensation of pain, while the periosteum might be analgesic. He quoted Oppenheim as saying that the sensation of pain in the deep parts may be dulled in the early stage of tabes. This dual sensation of the skin and periosteum would indicate that the cutaneous and periosteal fibers run through the cord in different paths, that one may be affected while the other is intact. An acute pathologic condition of the knee, with agonizing pain and fever, reported by Lemierre, proved at necropsy to be an acute, diffuse syphiloma of the joint.

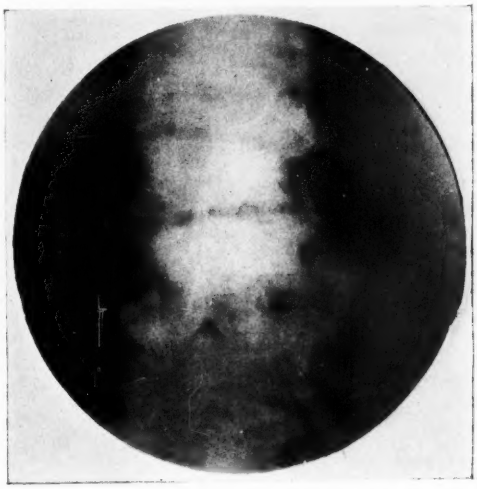

Fig. 1. Charcot's spine. The patient had been jammed by a cow six years before, and complained of pain in the knee, and later in the hips, but never in the spine. Note the marked destruction with the "chaotic" overgrowth characteristic of the Charcot's joints.

REPORT OF CASES

In the Mayo Clinic are records of 167 cases of arthropathies complicating tabes dorsalis, and three complicating syringomyelia. The youngest patient in the first series was twenty-three years of age, and it is interesting to note here that Elmer reported a pathologic intracapsular fracture of the neck of the left femur in a child of fourteen years with juvenile tabes dorsalis.

The history of trauma varied widely in degree, from definite crushing injuries and fractures to slight strains, such as turning the ankle. In many patients without a definite history of trauma the occupation predisposed to the type of injury that would result in an arthropathy, the greater number being farmers, artisans, railroad employees, laborers and woodsmen. Only three of the patients with arthropathy of the spine gave definite histories of trauma; two

had sustained the injury fourteen years before, and the third six years before examination; all had symptoms dating from their injury; all lesions were in the lumbar vertebræ.

Fig. 2. Charcot's shoulder. The only history of injury was a fall for a distance of three feet eighteen years before, the patient landing on the hands. The disease was painless in development. Note the marked disorganization of the joint.

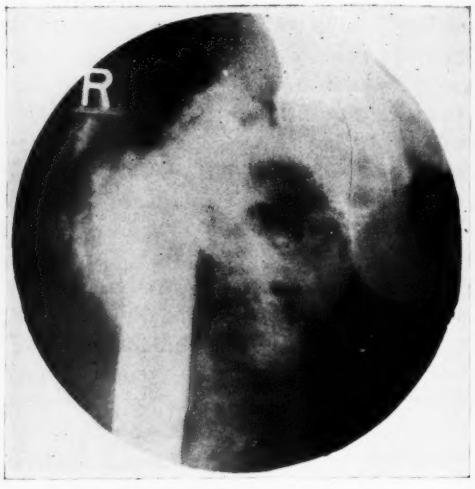

Fig. 3. Pathologic fracture in the femur without history of serious injury. Patient, aged forty-three years, a locomotive engineer, gave up his work only because of disability to carry weight of the limb.

DIFFERENTIAL DIAGNOSIS

For obvious reasons, the spine must be considered separately. In all cases in this series there was definite destruction of the vertebræ. This rules out the so-called osteoarthritides, which Goldsborough demonstrated were not osteal in origin, but due to calcareous masses surrounding the normal vertebræ. Destruction is associated with several conditions in the spine, so that it is necessary to turn to the clinical data and correlate them with the roentgen findings. With fractures of the spine there is a history of rather severe injury, followed by paralysis and disability. The roentgenogram, in the anteroposterior position, reveals a crushing of the vertebra (commonly one) with sometimes a lateral deviation of the fragments; the intervertebral discs are intact, above and below; if the injury has occurred a considerable time before, there is proliferation similar to that in osteoarthritis. The lateral view reveals wedging of the body, often a posterior dislocation of one fragment. Kümmel described a "spondylitis traumatica," the clinical symptoms of which simulate those of tuberculosis; the majority of such cases are found on X-ray examination to be stellate compression fractures of the bodies, softening and some absorption of the vertebræ occurring later. Tuberculosis of the spine clinically is attended with pain, often severe, and on movement or concussion the pain is often referred; the pain is relieved by recumbency, in contrast to that of tabetic arthropathy. Muscular rigidity is present, but is not marked as in arthritides. The roentgenogram reveals destruction of the body, and, commonly, the intervertebral disc. There is no evidence of proliferation of bone. In the lateral view there is marked wedging, due to the destruction of the anterior portion of the body. The deformity is almost always posterior. In cases of advanced tuberculosis, abscess will cast spindle-shaped shadows surrounding the affected vertebræ, or shadows of various shapes in the soft tissues below the lesion. Typhoid spine only slightly resembles

tabetic arthropathy. Clinically its onset is attended with a rise in temperature and pulse, and usually great irritability. Muscular rigidity is marked and the spine is carefully guarded against abrupt movements, twisting or jarring. Roentgenograms show a destruction of the intervertebral disc with marked proliferation of bone at the lateral margins of the vertebræ. In one case in which necropsy was reported, there was destruction of the disc and replacement by bony overgrowth.

Fig. 4. Charcot's knee. Two years before examination, a log had fallen across the knee; painless swelling developed, later the joint became flail. Note the wearing-down of the articular surfaces, and the subluxation of the joint.

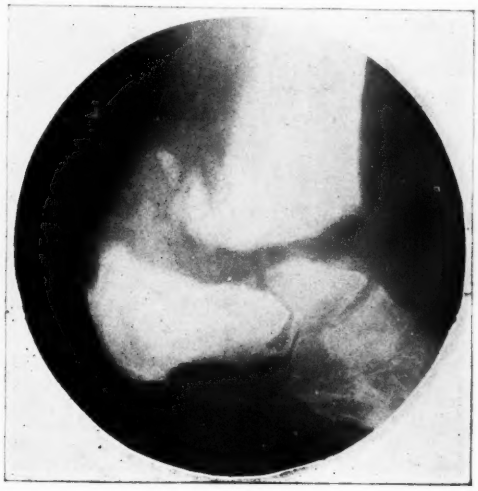

Fig. 5. Charcot's ankle. Nine years before examination, the foot had been caught under a moving sleigh. Painless swelling followed, the leg was finally amputated, and the patient developed a Charcot's joint in the other ankle.

Metastatic malignancy in the spine has one point in common with tabetic arthropathy: recumbency does not relieve the pain; however, the pain with metastasis becomes severe, even agonizing. Muscular rigidity is marked, and the patient becomes apprehensive of any movement. It presents two forms in the roentgenogram, the osteoclastic, in which the bone "melts" as ice does in the sun, and the osteoplastic, in which the bone is sclerotic. In the osteoclastic type, collapse of the bodies does occur, but the extreme decalcification of the bone and the absence of any attempt at proliferation of bone, differentiate it from tabetic arthropathy.

It is difficult to differentiate osteitis deformans (Paget's disease) and the osteoplastic type of metastasis in the spine. I have never seen collapse of the bodies in either of these conditions; in long-standing cases of Paget's disease a slight flattening of the bodies of the lumbar vertebræ has been noted. Lesions which clinically may simulate Charcot's spine have been reported as: actinomycosis (30) (occurring in but 2 per cent of all reported cases), acute osteomyelitis of the spine (9, 12), echinococcus cyst (11), and hydatid disease (15). I have seen but one echinococcus involvement of the spine, and roentgenologically it was easily differentiated from tabetic arthropathy.

One striking characteristic of the manifestations of syphilis as seen by the roentgenologist, is the disproportion between the clinical history and physical findings, and the extent of the lesion as revealed in the roentgenogram. In all other joints, as in the spine, the outstanding feature of Charcot's joint is the concomitant extensive de-

Fig. 6. Charcot's joint in the foot. Two years before examination, the patient had dropped a bar of iron across the foot. Painless swelling developed. The only disability was soreness after walking a long distance.

struction and marked proliferation of bone. Hypertrophic arthritis has been confused with tabetic arthropathy; the bone in this condition always retains its contour; there is usually some decalcification of the bone in contrast to the sclerosis of syphilis; marginal osteophytes and loose bodies in the joint may be seen in both. In the infectious arthritides one sees at times bizarre deformities of the hands and the feet which have been interpreted as Charcot's joints; the extreme atrophy of the bone with the absence of any suggestion of proliferation differentiates this condition. Fractures, particularly comminuted, in or around the joints, with secondary infection, or with exuberant callus, may be very difficult to differentiate, and the history must decide the diagnosis. As I have mentioned, pathologic fracture is common in cases of tabetic arthropathy. Acute septic processes in the hip-joint may cause marked destruction of the head and neck, and even the shaft, of the femur; the history will explain the roentgenogram in these cases.

The destructive arthritides are occasionally confusing; post-gonorrheal osteoarthritis is confined to the joint surfaces and usually does not destroy bone. Tuberculosis in the roentgenogram can be differentiated by the hazy appearance of the joint, due to the proliferation of the synovial membrane and sometimes to fluid in the joint. Increasing atrophy of the bone contrasts with the sclerosis of the bone in Charcot's joint. Tuberculosis of bone is more common in the young.

ARTHROPATHIES COMPLICATING SYRINGOMYELIA

In looking through the records of ninety-four patients with syringomyelia examined in the Clinic, I found that seventy-three had been examined by the X-ray; the roentgenologic findings were negative in forty;

TABLE I

ARTHROPATHIES COMPLICATING TABES DORSALIS

Joints involved	Right	Left	Bilateral	Total	Sex		Age (decades)						Wassermann reaction	
					M	F	20	30	40	50	60	70	Negative	Positive
Knees	32	29	5	66	50	16	3	6	25	27	3	2	44	22
Ankles	15	13		28	25	3	4	4	10	8	2		20	8
Hips	15	7	4	26	21	5	1	7	10	7	1		13	13
Spine				13	13			3	5	4	1		5	8
Feet	4	3	1	8	8		1	2	2	3			4	4
Shoulders	1	1		2	2			1		1			2	
Elbows	1	1		2	1	1	1			1			1	1
Wrists			1	1	1				1				1	
Fingers	1			1	1					1				1
Multiple				20	20		2	1	10	5	2		12	8
Total	69	54	11	167	143	25	12	24	63	57	9	2	102	65

TABLE II
DURATION OF THE LESION

Joints involved	Years														
	Less than 1	1	2	3	4	5	6	7	8	9	10	15	20	25	Indefinite
Knees	8	9	14	6	6	3	5	2	3	1	1	3	2	1	2
Ankles	7	8	4	3		1	2	1				2			
Hips	10	3	4	5			1	1		1					
Spine			2	1	3		2				1	2	1		1
Feet	2	2		1					2		1				
Shoulders	1						1								
Elbows		1					1								
Wrists					1										
Fingers				1											
Multiple	2	2	6	1	4	1	1	1		1				1	1
Total	30	25	30	18	14	5	13	5	5	3	3	7	3	2	4

TABLE III
DURATION OF SYPHILITIC HISTORY

Joints involved	Denied or not recorded	Years					
		1 to 5	6 to 10	11 to 15	16 to 20	21 to 30	31 to 40
Knees	29	3	1	3	17	12	1
Ankles	9	4	1	3	7	4	
Hips	9	2		1	12	1	
Spine	3	1	1		5	3	
Feet	3			3	2		
Shoulders	1				1		
Elbows	1				1		
Wrists	1						
Fingers					1		
Multiple	8		1		9	2	1
Total	64	10	4	10	55	22	2

TABLE IV
CLINICAL DATA ON CHARCOT'S JOINTS

Joints involved	Definite trauma or strain	Gradual onset, no record	X-ray diagnosis				
			Charcot's joint	Hypertrophic arthritis	Destructive arthritis	Fracture	Other lesions
Knees	25	41	36	17	6	2	5
Ankles	17	11	15	4	2	4	3
Hips	7	18	9	1	6	7	2
Feet	1	7	5		2	1	
Shoulders	1	1			2		
Elbows		2	1				1
Wrists		1	1				
Fingers	1		1				
Multiple	7	14	11		3	4	3
Spine	3	10	4	1	7		1
Total	62	105	83	23	28	18	15

spinal curvature or alterations in the vertebræ, not due to arthritis, but probably to weakness of the spinal muscles, was noted in fourteen, arthritis or lesions not attributable to syringomyelia in eleven, marked atrophy of the bones in three, and flexion deformities in the hands or feet in two. A man, aged forty-seven years, had a destructive lesion in the finger, which was diagnosed clinically as syringomyelia, with trophic changes (Morvan's disease). A woman, aged thirty-six years, presented an extensive destruction of the shoulder-joint, which was attributed to sarcoma; clinically this was diagnosed as syringomyelia with arthropathy. A man, aged twenty-three years, had a destructive arthritis of the metacarpophalangeal joint of the thumb, which was diagnosed clinically as an arthropathy associated with syringomyelia (Figs. 1 to 6).

SUMMARY

Charcot's joint is painless in most cases, developing rapidly, without appreciable cause. There is no fever, and no symptoms develop other than an instability of the joint. The condition is most frequently associated with tabes dorsalis; it may complicate syringomyelia, and similar lesions have been observed in cases of general paralysis of the insane, psoriasis, leprosy, anterior poliomyelitis, compression and destruction of the spinal cord, or following severance of nerves.

The lesion has been produced experimentally in healthy animals by section of the posterior (sensory) roots, thereby inhibiting the warning sense of pain in a limb, and it is apparently produced accidentally, chiefly by the movements to which the patients subject the affected members.

The roentgenogram reveals a simultaneous, enormous destruction of the articular surfaces and of the bones, with a chaotic hyperplasia of bone and cartilage in the surrounding tissues. The destruction, as seen in the roentgenogram, is entirely out of proportion to the clinical findings.

The incidence has varied from 1.75 to 6 per cent in different series of ataxic patients.

Tabetic arthropathies are more common in the lower extremities; arthropathies complicating syringomyelia more often affect the upper extremities.

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Gallstones.—The X-ray is a valuable means of diagnosing gallstones, from 30 to 40 per cent of them being visible. A negative X-ray examination is valueless. The shadow cast by gallstones is dependent upon their absorbability rate, the higher the rate the denser the shadow.

The author discusses the chemical composition of stones and shows why some are visible and others are not visible on the radiograph.

W. W. WATKINS, M.D.

The Value of the Roentgen Ray in the Diagnosis of Gallstones. Leon J. Menville. New Orleans Med. and Surg. Jour., June, 1924, p. 542.

Intestinal stasis and epilepsy.—Cuneo has established the fact that acidosis of local or remote origin plays a considerable rôle in the production of epileptic convulsions. The author has studied 27 cases of epilepsy very carefully. Thirteen cases were investigated roentgenologically. In every epileptic examined the clinical and laboratory evidences were very suggestive of chronic intestinal stasis and widespread mucosal catarrh of the intestine. Treatment was in every case primarily directed to the relief of the intestinal condition.

Fifteen cases have been sufficiently long under treatment to warrant deductions. Of this number, in five there has been complete arrest of attacks over a period from one to three years. Three cases have been much improved. Three other cases show a lengthening interval between attacks and a decrease in the severity of the attacks. Three cases showed no improvement, and one case died from pulmonary embolus following operation. Bromide and luminal were excluded from treatment. The author's treatment is directed to the restoration of the function of the gastro-intestinal tract, and particularly to the reduction of the septic catarrhal process. In addition, provision is made for a vitamin-rich diet, remineralization, endocrine and hormone reinforcement, and removal of septic processes. Where surgical relief of stasis is obviously necessary it is carried out.

SOLOMON FINEMAN, M.D.

Chronic Intestinal Stasis and Epilepsy. A. White Robertson. Brit. Med. Jour., Dec. 27, 1924, p. 1191.

Congenital defects.—This is a very comprehensive review of this anomaly, tabulating the 250 cases reported in the medical literature up to 1923, including three cases reported in the paper.

The principal pathology of this defect comprises total or partial absence of the radius, either unilateral or bilateral; the hypertrophied and curved ulna; congenital club-hand, usually radio-palmar in type; absence of thumb with metacarpal bone; general atrophy of affected extremity; limitation of joint movements. The defect is usually associated with other accompanying deformities. Diagnosis of the condition is usually not difficult, but ultimate verification must rest in radiographic findings.

W. W. WATKINS, M.D.

Congenital Absence of the Radius. Katsuji Kato. Jour. Bone and Joint Surg., July, 1924, p. 589.

CONGENITAL SYPHILIS OF THE BONES AND JOINTS[1]

By CHARLES C. DENNIE, M.D., Assistant Professor of Dermatology, University of Kansas
From the Department of Dermatology and Syphilis, Children's Mercy Hospital, KANSAS CITY, MISSOURI

THIS paper is based upon the examination and treatment of fifty cases of syphilis of the bones and joints and represents about 6 per cent of all cases of congenital syphilis treated by the writer. He does not intend to convey the impression that he has added anything new to either the diagnosis or treatment of these conditions, but he wishes to center attention upon some of the outstanding features that are commonly overlooked or disregarded.

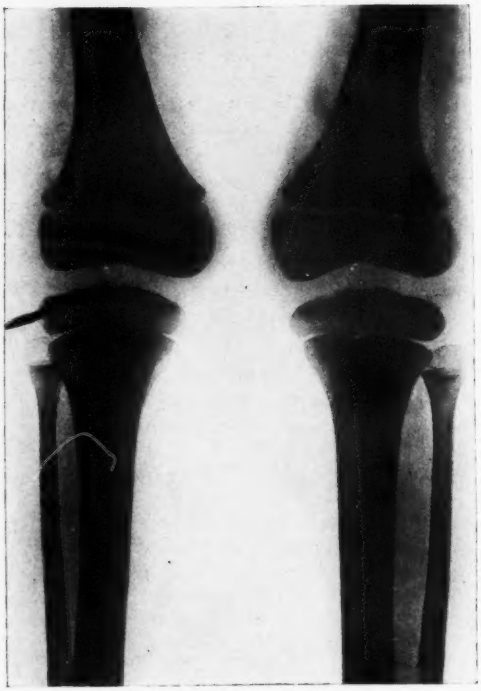

Fig. 1. Knee showing periarticular infiltration. Widened joint surfaces but no other pathology.

(*a*) Twenty per cent of these cases had a negative serology. Some investigators report as high as 40 per cent.

(*b*) Forty per cent had no sign of congenital syphilis excepting the bone condition and this characteristic finding was made possible only by the use of the X-ray.

(*c*) Of the 60 per cent who had some of the stigmata of congenital syphilis, only ten patients had interstitial keratitis and five had Hutchinsonian teeth, the most constant external finding being the saddle nose.

(*d*) The disease in the long bones was nearly always preceded by a history of trauma.

(*e*) In two cases the bone disease appeared at the termination of typhoid fever.

(*f*) Many of the cases started acutely and had the appearance of an acute osteomyelitis. Since nearly all of these children had a hyperplasia of the lymph and lymphoid tissues, infected tonsils, adenoids and sinuses were the rule; consequently the syphilitic bone manifestations may be and often are infected with pus-forming organisms from the very beginning and the train of signs and symptoms which follow are clinically indistinguishable from ordinary acute infective osteomyelitis.

(*g*) In a large percentage of cases all the other children of the family are apparently free from any signs or symptoms of congenital syphilis.

Since these facts are true, the following procedure should be followed in all cases of bone disease in children, excepting in those cases in which the physician feels absolutely sure that the case is one of infection or malignancy.

(*a*) A careful examination of the patient for the stigmata of congenital syphilis. An especially careful examination of all the rest of the family. Thirty per cent of the parents will show active manifestations of syphilis or evidence of its past ravages. The mothers are almost as often affected as the fathers.

[1] Read before the Radiological Society of North America, at Kansas City, December, 1924.

Fig. 2. Elbow showing same condition as Figure 1.

(*b*) The serology of the entire family is investigated, and will often confirm a rather shaky diagnosis.

(*c*) Radiographs of the long bones of the other children will often show that the child immediately preceding or following the patient has the characteristic thickened cortices of the tibiæ.

(*d*) Do not accept as conclusive the history of typhoid or any other acute infective disease, since these diseases often precipitate a latent congenital syphilis or activate foci which had already started. In two of this series of cases, bone disease immediately followed an attack of typhoid fever and was diagnosed typhoid osteomyelitis. The bone pictures in both cases were unmistakably those of congenital syphilis. One case had remained undiagnosed for thirty years. The latter responded to antiluetic treatment and was completely cured and the former was greatly improved when he left the hospital.

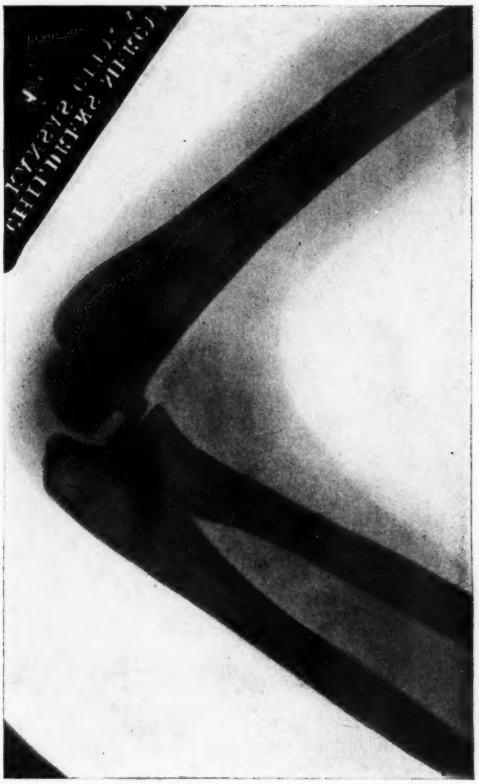

Fig. 3. Elbow showing periarticular infiltration which has existed for a long time. Rarefaction of joint is taking place which will result in destruction of joint if allowed to proceed.

(*e*) It is a well-known fact that individuals suffering from syphilis, whether it be congenital or acquired, are very susceptible to tuberculosis in some of its forms. It has happened that children who had joint disease coincident with tuberculosis of the chest, have had the involved joints immobilized in casts for months without result. Antisyphilitic treatment promptly cured the joints and did not activate the tuberculosis.

(*f*) A history of trauma should not be given too great a consideration.

(*g*) Where some evidence of syphilis exists and the case is not too acute, give the patient the benefit of a course of antisyphilitic treatment. These cases all respond

Fig. 4. Epiphysitis of the knee joint showing one epiphysis thicker than its fellow.

Fig. 5. Shows atrophy of epiphysis due to longstanding untreated periarticular infiltration. (This is decalcification of disuse.)

more rapidly to the arsphenamines than to the iodides and mercury.

CLASSIFICATION OF BONE AND JOINT DISEASE

I. *Periarticular infiltration, joint surfaces not involved.* Six cases with both knees involved and six cases with one knee involved. In two of these cases both elbows and both knees were involved; one case had paroxysmal hemoglobinuria.

The most common of joint diseases of syphilitic origin in children is periarticular infiltration. These children show marked enlargement of the joints, with a considerable degree of limitation of motion and practically no pain upon manipulation.

It has long been noted that bilateral involvement of any joints is very suspicious of congenital syphilis. When one examines these joints carefully one reaches the natural conclusion that marked bone changes have taken place. Such is not the case. A radiograph reveals no changes in the joint surfaces except some flattening, occasionally a thin line just above the epiphysis. The great change is around the joint; the capsule, tendons and the muscles about the joints are greatly thickened. This thickening is evidently due to lymphatic infiltration in the perivascular lymph spaces and to young connective tissue. This condition responds very rapidly to treatment. At the end of the first course the joint has returned to normal and no evidence of the disease exists excepting a slight enlargement, and this probably persists throughout life. Hydrops of multiple joints is not nearly so prevalent in congenital syphilitics as periarticular infiltration. The case of

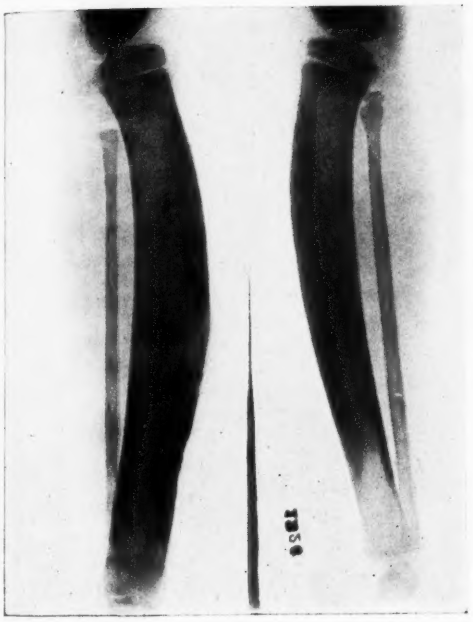

Fig. 6. Marked "sabre shin" showing tremendous thickening of the cortex and area of periostitis and osteitis in middle third of bone.

Fig. 7. Characteristic thickened cortex in congenital syphilitic with no other sign of syphilis. (Brother just older had characteristic syphilis of flat bone.)

paroxysmal hemoglobinuria did not respond to treatment, since he was given only the mercury and iodides. All of the rest were treated with intravenous arsphenamine.

II. *Syphilitic epiphysitis.* Four cases. In all joint diseases of this nature the knees are most often involved. They are always accompanied by periarticular infiltration. Clinically this manifestation is almost indistinguishable from the pure type mentioned above, but it is a far graver manifestation. A radiograph shows both epiphyses of the affected joint thickened, sometimes to almost double their original width, with marked rarefaction of the cancellous bone. In a large percentage of cases the joint surfaces are rough. In this type the epiphysis is probably the seat of secondary degeneration and the periarticular infiltration precedes it. Nevertheless, it is conceivable that if one permitted the periarticular involvement to progress, the epiphysis would finally become involved. These cases respond very slowly to treatment and more or less permanent ankylosis of the joint results. In some cases it was necessary to completely ankylose the joint in order to secure a usable limb.

III. *Osteitis, periostitis of the long bones, one or both.* Fourteen cases, twelve of the tibia, two of the humerus.

(*a*) Periostitis of the long bones is always attended by sharp pain. Palpation of the bone shows that it is thick and that it has lost its characteristic sharp edge. In nearly all cases of this type, there is a history of leg ache of months' or years' standing. The radiograph reveals a thickened periosteum, always accompanied by the characteristic thickening of the cortices. In this stage, one dose of arsphenamine will relieve the pain and clinically cure the patient.

(*b*) Osteitis plus periostitis. It is an evident fact that if one permits the involvement of the periosteum to continue, new bone cells will be laid down immediately

Fig. 8. Characteristic but rare syphilis of the long bone showing serrated character of the newly deposited osseous tissue.

Fig. 9. Periostitis and osteitis of the long bone secondarily infected.

under the involved part. This process will often continue until marked deformity is produced. Attention must be called here to a very characteristic but rare syphilitic bone process in which the bone is laid down under the periosteum in the form of scallops, giving the edge of the bone a serrated appearance. Coincident with this process, lime salts are laid down in the Haversian canals and in the lymphatic spaces between the cells, producing a bone of ivory hardness. Since the blood vessels and lymphatics are thus cut off, this diseased portion will either be

(*a*) cast off as a sequestrum;
(*b*) reabsorbed by the blood stream, producing a rarefaction, or
(*c*) become secondarily infected, producing an osteitis or osteomyelitis.

All three of these conditions will often exist simultaneously in a sabre shin. (*a*) and (*b*) will respond to antisyphilitic treatment. (*c*) will often do so, but surgical interference for the removal of sequestrum or infection will often be necessary. In either event energetic treatment should precede any surgical interference. Surgical procedure in these bones before treatment is disastrous. One patient in this series was operated upon before a diagnosis had been made and remained unhealed and unchanged for two years, causing him to become discouraged and to leave the hospital. The lesion remained unhealed in the face of energetic treatment.

The sabre shin which is so characteristic of congenital syphilis, when it does occur, is a permanent pathological condition in so far as the thickness and outward boundary of the bone are concerned.

Extensive and persistent leg ulcers in adults are often diagnosed as varicose or traumatic, while, in reality, a radiograph shows an unmistakable sabre shin. One patient, forty-two years of age, had an ulcer

on his leg which had persisted since the age of twelve, making its appearance after an attack of typhoid fever. Three times during the thirty years it had healed for a short period of time, but in each instance the man struck the leg and the ulcer made its

Fig. 10. Destruction of the head of the ulna in an infant three months old.

reappearance. A radiograph revealed a typical sabre shin. The Wassermann reaction is of no value in congenital syphilitics past the age of twenty years, since 80 per cent of them have a negative serology.

IV. *Multiple syphilitic bone involvement.* Six cases. In these cases the multiple involvement may be almost simultaneous, but, as a rule, one bone after another is involved. This may continue over a period of years before a diagnosis is made. In only two of these cases was there any coincident joint involvement, and in both of these it was an epiphysitis, one of the knees, the other of the hip joints. It was necessary to ankylose both in order to secure results. Three of these cases had absolutely no signs of congenital syphilis and the bone involvement was the only manifestation of this disease. Two of these cases have been under the writer's observation for nine years and two for five. There has been no recurrence of bone disease in any of the four. Four of them responded to treatment without surgical interference.

V. *Syphilis of the skull.* Two cases. Syphilis of the skull bones may take on one of two forms:

Fig. 11. Multiple dactylitis of the bones of the hand in an infant one year old.

(*a*) Permanent thickening of the entire skull, without rarefaction.

(*b*) Rarefaction of areas in the skull, with or without previous thickening.

In some instances the bulging forehead is not due to bowing out of the frontal bones, but is caused by the plastering of new osseous tissue on the frontal bone, so that the child really has a small skull cavity, although he may have a large head. (See Fig. 12.) The rest of the skull is markedly thickened, but the frontal bone is twice as thick as any other portion.

It is no uncommon thing for the rarefying type to extend into the sinuses and in some instances almost the entire outer bone will be destroyed. These cases have the characteristic emphysematous feel. When healing takes place a permanent depression is left.

VI. *Syphilis of the flat bones.* The nasal bones and palate are the most susceptible to syphilitic disease and are nearly always accompanied by single or double dacrocystitis. Treatment will stop the process if taken in time, but the disagreeable odor will exist for months and years after the process has stopped, since the injured

Fig. 12. Marked thickening of the skull (productive type.)

Fig. 13. Multiple areas of rarefaction in the skull of an infant three months old (destructive type).

tissue heals very slowly and the wide open space in itself will produce a fetid breath. Reconstruction of the nose is characterized by failure, and when a successful operation is performed, the nose often breaks down again. Energetic treatment must always precede reconstructive work and two prime factors must be borne in mind: (*a*) the area operated on must be free from infection and (*b*) no loose sequestrum must remain.

VII. *Dactylitis.* Two cases. Dactylitis is peculiar to infants and very young children, since they usually develop this condition before the third year and often do so before the first year. In all of the other cases of our series, with two exceptions, bone syphilis did not develop before the fifth year. Congenital syphilitics do not, as a rule, reach the late stage until after the fifth year. Dactylitis will heal spontaneously, leaving a permanent deformity. Syphilitic dactylitis is differentiated from the tuberculous variety because of the well-known fact that the tuberculous variety is situated near the epiphysis of the finger bones, while the syphilitic variety involves the shaft, and does not, as a rule, perforate to the outside. In some instances the shaft in the luetic variety has the appearance of a bone cyst, with spicules of bone crossing from side to side.

SUMMARY

1. Every case of bone and joint disease in children should be thoroughly investigated for congenital syphilis.

2. The history of trauma or previous infective disease should not be regarded as conclusive evidence that the pre-existing disease was the exciting factor in bone and joint disease in children.

3. The arsphenamines are the medication of choice in bone and joint disease of this character.

The writer wishes to thank Dr. Everett R. DeWeese, Radiologist, Children's Mercy Hospital, Kansas City, Mo., for his excellent radiographic work.

DISCUSSION

DR. P. M. HICKEY (Ann Arbor, Michigan): I was very much impressed by the first paper given, and also by Dr. Sutherland's demonstration. The wonderful wealth of clinical material which has been collected is so illuminatingly put at

our disposal for study. There is only one point that I would like to emphasize, in the first paper on Bone Syphilis, and that is the differential diagnosis between cases which, at our clinic, we are pleased to call subperiosteal gumma. Those cases oftentimes simulate an acute osteomyelitis or a neoplasm. I will simply give one case as an illustration. A boy ten years of age was brought to the clinic with the clinical appearance and manifestations of an acute osteomyelitis. The condition seemed so apparent that an incision was made, with the idea that pus would be found. It did not seem advisable to wait for X-ray or other diagnostic measures. However, no pus was found. He was then sent down to the X-ray laboratory, and I thought the most probable diagnosis was a sarcoma. It turned out to be a subperiosteal gumma, proven afterwards by the Wassermann and by the rapid improvement under anti-luetic treatment. One point, however, is prominent: in subperiosteal gumma there is usually an overhanging edge, quite characteristic in appearance from a neoplastic condition.

DR. L. T. LEWALD (New York): I would like to say that the connection with typhoid infection is rather striking in these cases. I have seen a latent typhoid infection in the bone as long as twenty-five years after typhoid fever. In this case we found the typhoid bacillus alive after twenty-five years. I would ask Dr. Sutherland how he explains the different types of lesions in the hip joint, one of which shows a great deal of production and the other extreme absorption of bone? If there is any explanation for this, I would like to know it. I have seen the absorptive type which was so strikingly different from the production type of Charcot joint that one would not think it was the same disease.

DR. SUTHERLAND (closing): Answering Dr. LeWald, I do not know of any adequate explanation. In looking through the series, I found a number, particularly among the films of the hip and knee, which showed only slight proliferation. There were several cases, particularly where the knee was the site of disease, which could not be absolutely differentiated roentgenologically. In such a dilemma, the only course is that which is always the safest in roentgenology, namely, to describe the roentgenograms and then consult with the clinicians. The discovery that the patient gives a history characteristic of Charcot's joint, makes the interpretation of the picture certain.

The important point in the history, as I have said, is the absence of pain in Charcot's joint. In these six patients, such marked destruction of bone without proliferation, if it meant anything at all, should have been eloquent of years of pain and disability; on the contrary they probably walked into the Clinic, and had most likely been carrying on their regular occupations. The roentgenogram alone gives a distorted reflection of the patient afflicted with Charcot's joint; it has to be corrected by the history.

Lateral view of antrum.—The position devised by this author is for a lateral view of the antrum without the superimposing of any other shadows. Patient lies on back, head tilted backwards at angle of 25 degrees, tube tilted to an angle of 60 degrees, tube brought down and as near to the uppermost mandible as possible. Antrum is shown without superimposed bony structures. Also shows upper and lower molars in normal position.

W. W. WATKINS, M.D.

A New Technic for Investigating Maxillary Sinuses by X-rays. Herman Besser. Med. Jour. and Rec., July 2, 1924, p. x (Respiratory Supp.).

Myelomatous tumors.—A myeloma of the head of the tibia containing much anisotropic fat-like material is described. Two morphologically similar tumors from tendon-sheaths are described for purposes of comparison. The presence in all these tumors of "foam" cells containing droplets of anisotropic fat-like substance —probably cholesterol ester—is adduced as evidence of the endothelial origin of all these tumors.

W. W. WASSON, M.D.

On the Significance of Anisotropic Fatty Substances in Myelomatous Tumors. S. C. Dyke. Jour. Path. and Bacteriol. (Gt. Brit.), Jan., 1924, p. 5.

CANCER OF THE LIP: ITS TREATMENT BY MEANS OF ELECTROTHERMIC COAGULATION, RADIUM, AND ROENTGEN RAYS[1]

By J. THOMPSON STEVENS, M.D., MONTCLAIR, NEW JERSEY

INTRODUCTION

CANCER of the lip is a subject of such great importance that no physician, surgeon, or radiotherapist can help taking an active interest whenever it is discussed. During the past great World War some 80,000 American soldiers lost their lives. During the same period, 180,000 persons in this country lost their lives from cancer. Standard surgical works tell us that 50 per cent of all cancers of the face are found upon the lip. In my own practice nowhere near 50 per cent have been located upon the lip, but this is probably due to the fact that I am not seeing these cases anywhere near as frequently as they occur. Statistics of the insurance companies show that one out of every ten deaths after the age of forty is due to cancer. With these facts before us, I feel sure that you will agree that we, as physicians, must stir ourselves into active combat with this dread disease. No one method of treatment has been found to meet the indications in an entirely satisfactory manner, therefore it is our duty to inform our patients as to the seriousness of their affliction, to advise generally combined methods of treatment, and to see that those who are selected to actually do the work are capable of meeting efficiently the indications as presented by the individual patient.

A cancer death is usually a most horrifying ordeal for the patient, his relatives, and friends. Death is preceded by agonizing pain which is eventually unrelieved by even huge doses of opium or its derivatives. There are sometimes discharges, the odor of which is unbearable by those living with the patient, sometimes marked deformity, and always great exhaustion and wasting of the patient's body. In cancer of the lip all of these symptoms are sooner or later present, though, of course, then the disease is no longer localized to the lip, — metastasis has taken place. Eventually the chest cavity even may be involved. The metastasis into the lymph nodes of the neck causes, in addition to the symptoms just cited, symptoms of pressure, and may even continue to actual suffocation. Given such a case, no matter if the best of radiation is given, no one should expect a cure to be obtained. The time for any marked palliation is generally past, no matter what method or combination of methods of treatment are instituted.

PROPHYLACTIC TREATMENT

As in cancer located elsewhere upon or within the body, if treated thoroughly and skillfully early in the course of the disease, there will be very few or no deaths from cancer of the lip. No patient, in my opinion, can be said to have received the maximum protection that it is now possible to receive all over the world, no matter what other treatment has been given, unless he has had intelligent radiation in the form of radium or roentgen rays or both. Statistical reports of the results obtained by modern methods in the treatment of cancer are piling up in the medical literature of the world. They clearly show that the time is past when a simple looking localized malignant growth or the premalignant lesion is to be treated as a simple pathological lesion and then forgotten. The prophylaxis of cancer of the lip demands the removal of all sources of chronic irritation, such as decayed, jagged teeth, trauma, the clay pipe, etc. Persistent fissures, cracks, ulcers, and wart-like lesions must not be treated by repeated caustic applications, but should be thoroughly destroyed and removed, preferably by means of electrother-

[1] From the J. Thompson Stevens Clinic for Radiation Therapy and Electrothermic Coagulation. Read by title at Annual Meeting of Radiological Society of North America, Kansas City, Dec., 1924.

mic coagulation. By this method of treatment almost without exception every patient will recover, the wound will heal soundly with a soft pliable scar, the deformity will be remarkably slight in comparison to the amount of destruction that has taken place, but, more important, the likelihood of cancer developing in the lesions will be practically *nil*.

PATHOLOGY

Squamous cell carcinoma, one of our most malignant types, commonly develops at sites where mucous membrane and skin meet, therefore it is the type found about the lips, particularly the lower lip. I have treated but one carcinoma of the upper lip to date. This, too, was of the squamous cell type. Very frequently it develops in the above-mentioned lesions, particularly if they are repeatedly irritated by caustics and the like.

SYMPTOMS

Cancer of the lip, as already stated, frequently begins as an excoriation, fissure or ulcer that will not heal; a tubercle covered by a thick crust that recurs as soon as it is picked off, or as a warty growth. The ulceration gradually spreads and deepens, the surrounding tissues being infiltrated and hard. In many cases the carcinoma begins as an ulcerating induration. The ulcer gradually assumes the typical appearance of an epithelioma, with an irregular, sloughing base and abrupt, everted edges. When irritated by the injudicious use of caustics, it tends to fungate and its growth becomes more rapid. At this stage it usually becomes quite painful, and nutrition soon suffers through the inability of the patient to take sufficient food, and a state of marasmus soon becomes evident, owing to repeated hemorrhages, ingestion of cancer débris, etc. General toxemia is by this time fully demonstrated by the patient's facies, and he sinks with increasing rapidity until death relieves him. As a rule the development is very gradual, and the glands of the neck are not involved early. Enlargement of these glands and even their induration do not necessarily imply infiltration with carcinoma. Glands examined immediately after removal have been found free of malignant changes; but there is no doubt that such glands constitute foci for carcinomatous degeneration and that they should be looked upon as definite metastases.

DIAGNOSIS

Chancre of the lip sometimes makes the diagnosis somewhat difficult. Carcinoma occurs almost always in men; chancre is more frequent in women and may occur at any age, while cancer seldom occurs before the fortieth year. The progress of cancer is slow and the lymphatic glands are not involved until late; chancre advances rapidly, lasts but a few weeks, and the glands are soon affected. Finally the secondary manifestations appear in syphilis and greatly improve under specific treatment. Cancer progresses regardless of all internal remedies. The Wassermann test is positive in chancre, negative in cancer.

ELECTROTHERMIC COAGULATION

TERMINOLOGY

Unfortunately, as in other branches of medicine, we find here a multitude of terms used to designate one and the same procedure. This is called surgical diathermy, fulguration, surgical thermopenetration, desiccation, endothermy, endothermy knife, radioknife, etc. If we are to use the term "endothermy," it must be preceded by the word "surgical," the same as is done when it is called "diathermy." However, to my mind there are some very important reasons why all such terminology must eventually give way to *electrothermic coagulation*. This term at once conveys to one's mind the fact that there is a production of heat by an electric current of sufficient intensity to coagulate the tissues to which the current is applied. Furthermore, two Philadelphia physicians have probably had more to do with the broadcasting of the details of this treatment than anyone else. For approximately twenty years they have

called it "electrothermic coagulation," and I have used the same term during the past ten years. I refer to the work and writings and Dr. William L. Clark and Dr. George E. Pfahler, and it is my plea that their terminology be used. Recently, in a personal letter from Dr. Howard A. Kelly, who enjoys an enviable international reputation as a surgical authority, I have the following in favor of electrothermic coagulation in the treatment of accessible malignant disease: "I call it the new surgery; it is the biggest thing that has come into the surgical realm for many a year. We are using it every day and it is invaluable in some of the cases, either where radium fails or where the use of radium has so far altered the tissues that it is impossible to go ahead with it. One beauty of this form of treatment is that it can be so sharply and definitely localized and can be used repeatedly in the same area and that the wounds consequently are generally not at all painful and healing is so beautiful."

Electrothermic coagulation is the localized production of heat in the tissue from within, which is caused by the many oscillations of a high frequency current and is applied to the tissues by means of a pointed electrode. As compared with excision it has the enormous advantage, in accessible cases, of *destroying the malignancy before it is removed.* It is impossible to overestimate the value of the fact that with coagulation the growth is removed as a dead mass of tissue instead of as a mass of viable cells. This, plus the fact that the lymphatics and blood vessels supplying and draining the affected area are closed, tends to remove the possibility of mechanical metastasis. As compared with all other methods of cauterization by heat in coagulation, the active electrode is cold at all times. Heat develops in the tissues treated because of their resistance to the flow of the current. Therefore it is progressively more penetrating the larger the amount of current used and the longer it is applied. The actual cautery, as we all know, rapidly heats the tissues to which it is applied to a very high temperature, the tissues being charred if the heat is applied long enough. However, the actual cautery does not produce sufficient heat deep down in the tissues and, therefore, the results in the treatment of accessible malignant lesions by means of the actual cautery fail to compare with those obtained by means of electrothermic coagulation.

TECHNIC

In cases of cancer of the lip that are absolutely localized, also those presenting premalignant lesions, the treatment is begun by a complete and thorough destruction of the lesion by means of electrothermic coagulation. This is a surgical operation and must be completed at one sitting if best results are to be obtained. For the smaller lesions the Oudin or monopolar current is used. The proper amount of current to use must be learned by experience. Valuable practice can be obtained by treating a piece of meat. The pointed electrode or applicator is held close to the tissue so that sparking occurs. The lesion is completely encircled with a necrotic, dried out, or desiccated wall of proper depth, caused by the discharge of the sparks into the tissues. This desiccated wall must be placed in the healthy tissues some distance from the actual lesion. It is the most important part of the treatment, because, if properly done, metastasis will be prevented; if not properly done, metastasis is almost sure to take place and failure to save the patient's life is the result. Then the lesion itself is completely desiccated by sparking, as above. If necessary, the needle may be run into the lesion to produce deeper desiccation. The desiccated tissues are next removed with a curet and if all of the unhealthy tissues have not been desiccated, further desiccation, not at some future time, but then and there at the one sitting, is demanded. If desired, the work can be completed in so far as surgery is concerned by a dressing of collodion and cotton. However, I have found that healing is more rapid if left exposed, and, since the wounds are generally

not large enough to be objectionable, this is the usual procedure.

For the larger lesions, those involving the lip deeply, the d'Arsonval or bipolar current is used. With this current deep heat in sufficient quantities to destroy any tissue of the body, including bone, can be obtained. Therefore, in its use about the lip care must be exercised, otherwise the jaw bone may be injured or even destroyed. Likewise, if the jaw bone is diseased, no method can exceed it for efficiency in the removal of the affected bone. A large pad or metal electrode is connected with one pole of the machine, the electrode being placed usually under the buttocks of the patient. This electrode must be well wetted, preferably with saline, else the patient's skin may be burned at this point. To the other pole of the machine the active electrode is attached. The point is then held in contact with the tissue to be destroyed and the current is turned on. No rule can be given for the predetermination of the amount of current to use. There is no guide that can be advised save that gained through experience with this method of operating. The coagulation at one point is completed when the tissues are dead white or coagulated, and the current is switched off just before sparking begins. As already stated in the preceding paragraph the coagulation begins well out in the healthy tissues, the diseased area being completely walled off from the healthy tissues by the coagulation wall, and finally by painstaking care the carcinoma itself is destroyed and removed. All of the disease must be destroyed at the one sitting, otherwise the patient's chances for ultimate recovery are jeopardized. The operation is completed by the application of a suitable dressing of collodion and cotton or gauze.

RADIATION THERAPY

The radiation therapy of any carcinoma is a time-consuming operation. Unless one is prepared or can afford to devote several hours to each individual patient, he had better not take up this part of the treatment. As has already been said, each patient suffering with a malignant lesion must have radiation therapy as a routine, otherwise that patient has not had the best of care. Often I think that many times better results might be obtained if this work were in the hands of a qualified physicist. The points to be considered are for the most part physical. Care must be taken in the actual application of the rays in any such doses as those about to be advised, otherwise there is danger of doing more harm than good. Any less dosage cannot be thought of, for obvious reasons. Great skill, care, and thoroughness must be the watchwords. One may think he is actually producing by crossfiring the proper intensity of radiation at all points. Many times, I am sure from what I see, too low an intensity was produced at some point in the radiation field and too high an intensity at some other point. Of course, this could not have occurred had the operator had the necessary training in the physics of the subject. At all times we must remember that the best equipment does not necessarily make one a qualified radiotherapist any more than a fine collection of surgical instruments will make their owner a wonderful surgeon.

In the radiation of carcinoma of the lip the radiations are given in such a way as will efficiently ray the site of the disease and all of the lymphatics, both superficial and deep. For the localized effect radium element in the form of needles of five or ten milligram capacity is used. These needles are buried deeply into the base of the coagulated area one or two centimeters apart and are left in place for sixteen hours. If there are any metastatic glands present, radium needles, using the same technic, are buried deeply into them.

No matter how much radium is available one must use the roentgen rays to properly ray the lymphatics draining the site of any carcinoma. It is imperative that the physician himself or a specially trained technician sit in constant attendance during the entire operation of the machine. In no

other way can the amperage and voltage be kept constant. This is a most important point if anywhere near the intended dosage is to be correctly given. Both of the above factors are apt to vary often within wide limits, and if allowed to go on without being corrected by the operator too much radiation or too little will be the result. Any good results obtained without this constant presence of the operator are probably accidental.

In my clinic, in addition to the usual history-taking and physical examination, every patient is examined with the roentgen rays for metastasis into the chest. Films are made in the usual posterior-anterior position, also laterally, special attention being given to the upper mediastinum and sternum. Whether or not this roentgen examination shows any metastasis, the radiation begins with a thorough radiation of the upper half of the mediastinum, using anterior, posterior, and lateral ports in a sufficient number to produce, with the factors used, an intensity in the mediastinum equal to three-fourths my erythema skin dose, or 150 electrostatic units. The factors for this work are: 4 ma., 210,000 volts, 0.5 mm. Zn. plus 3 mm. Al. filter, at a distance of 42 cm. The skin of any one port does not receive more than 150 electrostatic units of dosage. The clavicular and cervical regions are radiated with the same factors but at a focus skin distance of 32 cm., using the same dosage to each port. The submaxillary region and the lip are radiated with the 140,000 volt rays through 0.25 mm. cu. plus 3 mm. Al. at a focus skin distance of 32 cm., using 150 electrostatic units of dosage over each of the necessary ports of entry. The entire procedure is repeated in two weeks' time.

RESULTS

The results of this method of treatment appear to warrant its being the method of choice in the treatment of carcinoma of the lip. Similar results are reported by Clark, Pancoast, and Pfahler, who were probably the first to report their results from technic similar to that described above. Up to December 31, 1923, thirty-eight cases of proven carcinoma, absolutely localized to the lip, were treated. All save one made uneventful recoveries. This one, a patient of Dr. Walter Reick, for some reason developed a submaxillary gland which resisted both the roentgen and radium rays. The overlying tissues were incised down to the tumor, which appeared to be composed entirely of scar tissue and which was firmly adherent to the jaw bone. The entire tumor was thoroughly destroyed through the open wound by means of electrothermic coagulation. The wound was left open and to date has never healed. Personally, I am of the opinion that the heat of the coagulation has destroyed a portion of the jaw bone or periosteum. However, roentgen examination by Dr. Charles F. Baker failed to show either. In any event, there is now a large discharging sinus which is anything but satisfactory. The lip itself healed normally, and I am almost sure that there are no carcinoma cells present.

Twenty-two hopeless cases were treated, four of whom are still alive and free from any evidence of their former disease. These cases at the time of my initial treatment presented large, deep ulcerations with metastasis into one or both submaxillary and cervical glands. They had been treated by irritating caustics, repeated curettings, or by inefficient doses of roentgen or radium rays. Twelve had been operated on by some of our ablest surgeons but had had no pre- or post-operative routine radiation. No one should expect a single five-year cure to follow the best of combined treatment in this group, though I suppose that partial relief of some of the symptoms for a time makes the work well worth while. Particularly is it discouraging to get patients who have had inefficient radiation, with the hope that perhaps more efficient radiation will produce the desired results. This group seldom produces a result which might be called even a palliation.

CONCLUSIONS

1. The prophylaxis of cancer of the lip, the pathology, the symptoms, and the diagnosis are reviewed at some length.
2. The technic of treatment by means of electrothermic coagulation, radium, and roentgen rays is described in considerable detail.
3. The results obtained show that practically all in the group presenting localized cancer should be cured if treated thoroughly and skillfully by means of electrothermic coagulation, radium, and the roentgen rays.
4. The results obtained show that practically all in the group presenting deep ulcerated malignancies with metastasis are doomed to die of their disease, no matter what is done.

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X-ray in urology.—The increasing dependence on radiology for diagnosis is nowhere more noticeable than in the field of urology. With the use of the Bucky diaphragm, 96 per cent of urinary calculi should be shown. The fluoroscope has had limited use in the hands of these authors, the exposure at two angles during pyelography being the technic used by them. They have substituted the injection of oxygen for opaque media into the kidney pelvis in many cases, as it causes less pain and reaction.

W. W. WATKINS, M.D.

Roentgen Diagnosis in Urology. Robert H. Lafferty and C. C. Phillips. Sou. Med. Jour., Aug., 1924, p. 623.

Grouping of cases of cancer of cervix uteri.—This paper is a summary of results in 416 cases of cancer of the cervix treated by radiation. Most of the cases were treated by the application of radium in the cervical canal, in combination with high power roentgen ray. The cases are classified into four groups. Group I contains all lesions of the cervix which were entirely confined to the cervix, with no extension into the fornices or vaginal mucous membrane. Of 15 cases in this group, 13 have been well for periods of from six months to four years. In Group II were placed all cases farther advanced in which a portion or all of the cervix was involved, with extension to the mucous membrane and walls of the vagina. Of 30 cases in this group, the results were undetermined in three. Fifteen cases, or 56 per cent, have been clinically well for periods varying from three months to three years and eight months. Five cases are reported as unimproved and six have died. The average length of life for these cases was sixteen months, the longest palliation being two years and three months, and the shortest seven months. Group III contains all cases in which the cervix and the mucous membrane of the vagina were involved, with beginning infiltration of one or both broad ligaments and moderate fixation. Twenty-five of these cases, or 27 per cent, were clinically well for periods varying from one month to three years and six months. Eleven cases were improved, 29 unimproved, and 27 have died. The average length of life was nine and one-half months, the longest palliation being three years and ten months and the shortest one month. Group IV contains all cases which were exceedingly far advanced, in which the cervix, upper end of the vagina and both broad ligaments were markedly infiltrated, causing complete fixation of the uterus. There were 253 cases in this group and the results were undetermined in 45 cases. Five current cases were reported as improved, 95 were unimproved and 106 have died. The average life for these cases was eight and one-half months, the longest palliation being three years and ten months and the shortest one month.

The author concludes that the results in the treatment of cancer of the cervix in the so-called operable class (Groups I and II) are as good or better than the surgical treatment. In farther advanced cases the results have surpassed what could be expected by surgical treatment.

J. D. CAMP, M.D.

Summary of the Clinical Results after Irradiation of Cancer of the Cervix Uteri. Bernard F. Schreiner. Am. Jour. Roentgenol. and Rad. Ther., Oct., 1924, p. 367.

SIGNIFICANT CELLULAR CHANGES OBSERVED IN IRRADIATED TISSUE, ESPECIALLY OF CANCER OF THE RECTUM[1]

By HARRY H. BOWING, M.D.

Section on Radium and X-ray Therapy, Mayo Clinic, ROCHESTER, MINNESOTA

FROM June, 1919, to June, 1924, forty-three cases of cancer of the rectum were resected at the Mayo Clinic, in which radium alone or in combination with roentgen rays was applied prior to operation. Thirty-four cases were treated as a pre-operative procedure, following a short interval after permanent colostomy. Nine cases were treated elsewhere, and in only one of these was a colostomy made prior to the irradiation.

This small group of cases was studied for the special purpose of observing, if possible, those changes resulting from the application of the therapeutic rays of radium, and the X-ray. A similar study of cancer of the breast was made (2), which proved to be a substantiation of the work of Alter on irradiated cancer. MacCarty and Broders have reported data on cases of unirradiated cancer. It seems evident that cellular changes can be abundantly produced in malignant tissue, which reduce or inhibit the malignant process.

Microscopically, the cellular changes in irradiated tissues seem to be identical to those which the body naturally produces in its effort to rid itself of malignant disease, and would indicate that the mechanism was similar. A better understanding of this mechanism should afford means for improving technic, and methods of dealing with the disease.

It is not uncommon for radiotherapists to find that cancer of the rectum has been favorably modified, and occasionally that the visual and palpable manifestations of the disease have entirely disappeared. There are cases in which careful microscopic section of the tissue removed does not reveal any active cancer cells. Not only is there local improvement, but a gradual, steady, systemic improvement. Various factors may account for such improvement, but only the probable mechanism underlying the reduction in malignant tendencies in tumor tissue, with and without irradiation treatment, will be discussed here.

Broders, as a result of summing up or averaging observations on unirradiated tumor tissue, has graded tumors so as to furnish a valuable index to the degree of malignancy. The surgical staff of the Clinic, in view of the practical aspects of such gradation, now use it as a guide to effective surgical procedures. In order to treat neoplasms scientifically it is essential that these important tissue changes should be recognized. Since these factors normally occur in untreated cancer tissue, although at a comparatively slow rate, and in varying degrees, a study of irradiated tissue in which this natural process had been produced at a comparatively rapid rate seemed pertinent. This phase of the study, as has been mentioned, cannot be overemphasized.

A few years ago the physicist was in much the same position as that of the pathologist to-day. It was not until the physicist's knowledge became practical that the art of radiotherapy advanced; the perfection to which the mechanical phase of radium and roentgen-ray treatment has reached can be attributed in great measure to his efforts. The physician who employs these agents must have a liberal knowledge of the fundamental physical phenomena controlling them.

Information now received from the pathologist concerning his diagnosis of malignancy is incomplete; he must furnish more definite information concerning the degree of malignancy found in a given

[1] Read before the Radiological Society of North America, Chicago, June, 1924.

case; both factors are equally important. Thus his specialty has come to occupy a definite place in the therapeutic management of a case. Physicians treating malignant disease must have a working knowledge of this phase of the work, and the art of radiotherapy will be greatly improved and further advances assured when these factors are taken into account at the time treatment is outlined and applied. It is not within the scope of this study to discuss details concerning the factors which form the basis for this grading, but rather to record the data in the forty-three cases observed, and compare them with Broders' and MacCarty's data on cases of malignancy in which pre-operative treatment by radium was not given.

Grossly, the tumors removed at operation in this series of cases were large and bulky. Very few, if any, could be designated early operable lesions. The tumor was divided longitudinally, and a section for microscopic examination was taken from the margin and the center of the malignant tissue. This procedure furnished material fairly representative of the bulk of the tumor.

TABLE I

TYPES OF TUMORS
(BRODERS' CLASSIFICATION)

	Cases	Per cent
Adenocarcinoma	37	86.04
Colloid carcinoma	4	9.30
Squamous-cell carcinoma.	1	2.32
Not determined	1	2.32
Total	43	

From the standpoint of a radiotherapist, it is gratifying to know that so high a percentage (86.04) of tumors are of the adenocarcinomatous type, for as a rule a response to treatment can be expected. Squamous-cell cancer in the rectum metastasizes rapidly to the inguinal glands, and the result is usually that of disseminated cancer. The primary tumor can be modified and made less malignant, but the multiple and widely distributed secondary growths are fatal. Colloid cancer, by producing colloid material, seems to bring about atrophic change in the cell, possibly as a result of pressure, and death of the malignant parenchyma eventually ensues. Whether or not this function can be accelerated is highly problematic.

Owing to the previous exposure to the therapeutic rays, the true malignant character of the tumor was masked, and therefore the possibility of error must be considered in the grades recorded. The grades as a whole check satisfactorily with Broders' findings, so that it is reasonable to assume that this error is not large.

The cases studied by Broders were selected from various locations, such as the genito-urinary tract, the lip and skin (Table II). Allowance for variations, due to anatomic location of the malignant growths, should of course be made in considering the data, but it is clear that the grade of malignancy has a direct bearing on results, regardless of the location; in this point, particularly, radiotherapists are interested.

As will be seen in Table II (Broders' series), the results of operation without pre-operative treatment were good in 92.2 per cent of the untreated Grade 1 tumors, whereas the results were poor in 89.2 per cent of the untreated Grade 4 tumors. This high percentage of poor results in Grade 4 tumors shows why many surgeons regard this degree of malignancy as inoperable. However, in the series of tumors of Grades 3 and 4, which were irradiated pre-operatively, the results were poor in only 57.89 per cent. Although the series is probably too small a one on which to base an accurate opinion, this improvement of 32 per cent certainly indicates that the effects of pre-operative radium treatment are noteworthy in cases of highly malignant tumors (Grades 3 and 4). Moreover, the cells of highly malignant tumors divide rapidly, and at this stage are most vulnerable to the therapeutic rays. It may be remarked that

TABLE II

UNTREATED CASES (BRODERS)

Post-operative results	Grade 1			Grade 4		
	Good	Fair	Poor	Good	Fair	Poor
Cancer of the genito-urinary tract	10	1	1	10		72
Cancer of the lip	43	2				4
Cancer of the skin	13	1				7
Total	66	4 (92.9%)	1	10 (10.8%)		83 (89.2%)

TREATED CASES (BOWING)

Post-operative results	Grades 1 and 2			Grades 3 and 4		
	Good	Fair	Poor	Good	Fair	Poor
Cancer of the rectum	9 (69.2%)		4 (30.8%)	11 (57.89%)	4	4

TABLE III

CANCER OF THE RECTUM

Cases	Untreated (MacCarty)		Treated (Bowing)	
	Years	Per cent	Years	Per cent
Average length of post-operative life	1.47		1.76	
Frequency of differentiation		85		100
Frequency of lymphocytic infiltration		57		100
Frequency of fibrosis		75		100
Frequency of hyalinization		2		7.69
Frequency of differentiation and lymphocytic infiltration		56		100
Frequency of differentiation and fibrosis		70		100
Frequency of differentiation and hyalinization		2		7.69
Frequency of lymphocytic infiltration and fibrosis		47		100
Frequency of lymphocytic infiltration and hyalinization		1		7.69
Frequency of fibrosis and hyalinization		2		7.69
Average length of post-operative life				
With differentiation	1.54		1.76	
Without differentiation	1.08			
With lymphocytic infiltration	1.57		1.76	
Without lymphocytic infiltration	1.31			
With fibrosis	1.53		1.76	
Without fibrosis	1.29			
With hyalinization	2.33		0.59	
Without hyalinization	1.44		1.82	
With differentiation and lymphocytic infiltration	1.59		1.76	
Without differentiation and lymphocytic infiltration	0.71			
With differentiation and fibrosis	1.58		1.76	
Without differentiation and fibrosis	1.15			
With lymphocytic infiltration and fibrosis	1.65		1.76	
Without lymphocytic infiltration and fibrosis	1.17			

whereas the results for tumors of Grades 3 and 4 were decidedly improved by preoperative irradiation, they were comparatively unfavorable when similar therapeutic measures were employed for tumors of Grades 1 and 2, since good results were obtained in only 69.2 per cent as compared with Broders' 92.2 per cent. This may be owing to the large size of all the tumors in the present series, and possibly to the ana-

tomic position. It may indicate that tumors of Grades 1 and 2 are best treated by surgery alone.

In 1922, MacCarty studied the factors which influence longevity in cancer. Included in his cases were 102 of cancer of the rectum. The specimens were studied to determine the frequency and possible influence of lymphocytic infiltration, fibrosis, hyalinization, and cellular differentiation on post-operative longevity. Since he does not classify the tumors according to Broders' grading, the results in this series cannot be compared on that basis. However, in Table III are compared the factors of longevity and of lymphocytic infiltration, fibrosis, hyalinization, and cellular differentiation. Although the present series of cases is smaller than MacCarty's, there is a certain significance in the comparison, and it is hoped that it will stimulate others to add to the data relative to pre-operative irradiation in cases of cancer of the rectum. The factors of differentiation in the parenchymal cells of the tumor, and in the lymphocytic, fibrotic and hyaline changes in the stroma or supporting matrix, are no doubt intimately combined, and represent or afford visualization of the tissue effects of the intrinsic cancer-resistant mechanism at work. When present, they are the markers which indicate that the patient is putting up a fight against the invading malignant cell. The findings in the irradiated group compare favorably with MacCarty's. The tissue changes brought about by the treatment are definitely shown by the increase in the post-operative years. The frequency of differentiation, lymphocytic infiltration, fibrosis, and hyalinization are all greatest in the treated patient.

The average length of life in MacCarty's series of cases was 1.47 years; in the present series, 1.76 years. The highest percentage (85) in MacCarty's series was related to the factor of differentiation, and the lowest (2) was that of hyalinization. Percentages in the present series are persistently increased in every combination. This no doubt indicates that the natural defense mechanism was brought into action. When the percentages are studied as a whole, they demonstrate clearly that the factors influencing longevity in patients with cancer of the rectum can be enhanced or accelerated by the application of radium (Table III).

Of the thirty-three patients (94.28 per cent) who were traced after leaving the hospital, eighteen (54.54 per cent) are living, and fifteen (45.46 per cent) are dead. Ten (55.55 per cent) of the eighteen patients are living three years after the first application of radium, two (11.12 per cent) less than one year, and six (33.33 per cent) less than between two and three years.

The surgical mortality (18.6 per cent) was too great in the treated series; this may be attributed to post-influenzal infections, especially prevalent in 1919, and to operations performed too early, when the effects of treatment on the tissues were most severe. Most patients were operated on less than two weeks after the first application of radium, two or three treatments having been given. The reaction was, therefore, at its height. A longer interval is now allowed.

TECHNIC OF ADMINISTERING RADIUM

No distinction was made between the applicator containing the radium sulphate and the radium emanation (radon), provided the measurements of energy content were relatively equal. When the radon was employed, the brass filter used was equal to a filter of 0.5 mm. silver. The Universal silver tube applicator with walls 0.5 mm. thick, and containing 50 mg. of radium element (sulphate), was the applicator of choice. This was usually placed in a thin brass shell with a wall about 0.3 mm. thick, one end of which was closed and soldered to a lead stem which made it possible to direct, as well as to fix, the applicator into position. The lead stem was about 20 cm. long and could easily be bent to suit the contour of the buttock or sacral area; it

was held in place with adhesive plaster. Ordinary motions in bed will not displace this applicator. Over the brass shell was placed a para rubber tube, wall 1.5 mm. thick and about 2.5 cm. long, allowing the end to protrude beyond its end about 2 or 3 mm. The contracture in the rubber tube insured the fixation of the Universal radium tube in the shell; it also furnished a soft tip, for minimizing trauma in placing the applicator.

The dose was planned to be given in two or three applications of from twelve to fourteen hours each, and repeated in two or three days. The total dose was arranged so that the posterior resection would follow from ten to fourteen days after the first application. Five patients were given the average total treatment of 750.4 mg. hours; twenty-two were given the average total treatment of 1,614.0 mg. hours, and nine were given the average total treatment of 2,499.77 mg. hours.

The interval between the first application and the operation was less than two weeks for fifteen patients; more than two weeks and not greater than four weeks for six; the interval was not less than six weeks and not greater than seven weeks for three, and much longer, varying from fifteen to sixty-seven weeks for nine. The chief reason for this long interval was the patient's poor general condition, which added greatly to the risk of the operation. Following this interval, patients regained much of their strength, and thus the posterior resection was warranted. In eleven cases (25.58 per cent) the gross effects of the tissue changes noted at operation were recorded as "edema," "oozing," "fibrosis," or "fixation." In four surgical records (9.3 per cent) it was noted that the operation was made more difficult by the effects of the treatment.

All of the tumors were large and ulcerated and many were bulky and fixed before treatment was begun, so that some of the complications may have been due to the character of the disease, although since most of the patients were operated on within the two-week interval, it is reasonable to conclude that the altered tissue added to the surgical difficulties.

It is difficult to determine the most satisfactory treatment interval since much depends on the dose and the individual response. All of the effects of the treatment should have disappeared and the secondary infection and ulceration be reduced to a minimum before surgical intervention is undertaken. It can be assumed that at the end of six or eight weeks the patient should be re-examined, at which time operation, or a longer treatment interval, should be decided on.

DISCUSSION

From the foregoing it would seem that the healing process following radiotherapy, in cases of cancer, may be divided into two phases: the changes in the parenchyma cell, and the changes in the stroma or supporting matrix. In the first of these, provided the exposure is destructive, necrosis is the characteristic feature; if the exposure is non-destructive, differentiation occurs in the parenchymal cells, and the range of differentiation is evidently an inherited distinctive feature, related to either form or function. The character and amount of reaction noted in the matrix are no doubt dependent on the intensities employed, as well as on the susceptibility of the individual, and are characterized by a combination of ordinary sequences: (1) invasion of a leukocytic infiltration; (2) fibroblastic changes resulting in the formation of a very cellular fibrous tissue, and later, of a very dense non-cellular tissue, and (3) formation of hyalin. Eventually, a definite degenerative change is indicated by the deposits of calcium; this demonstrates that, when the purpose of the reaction in the supporting matrix is accomplished, degeneration occurs, and that it is no longer of value in the restorative process.

As yet, very little has been done to determine the quantity and quality of therapeutic rays necessary to bring about this satisfactory result in arresting neoplastic disease

through differentiation rather than through destruction, by imitating or stimulating the natural defense processes observed in untreated neoplastic tissue.

The science and art of radiotherapy will be greatly advanced by the determination of these as yet unknown factors. In the meantime, we should be studious and observant, and endeavor in every case to give individual treatment.

CONCLUSIONS

1. This study is intended, primarily, to record the tissue changes in cases of cancer, and, if possible, to correlate observations.

2. The natural defense mechanism or the factors influencing the longevity of patients with cancer can be greatly enhanced or accelerated by the application of the therapeutic rays of radium.

3. The treatment interval between the first application and the operative procedure should be sufficiently long to permit the maximum of tissue repair, thus reducing to a minimum the surgical difficulties, the great chance of secondary infection in the operative field, and the malignant characteristics of the tumor.

4. The pathologist can be of great service in the therapeutic management since his opinion furnishes an extremely valuable index to govern the best method of procedure. A careful biopsy can be done just before the application of the first radium treatment with very little, if any, risk.

5. It is hazardous to set up a therapeutic framework in the management of patients with cancer by a combination of radium therapy and radical surgical measures. The best results are possible only by individual treatment with a sufficient time interval between the first radium application and the operation for all the important effects on the tissue to have occurred and subsided. Such time is estimated in weeks rather than days.

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Radiation of inoperable cancer.—The inoperable cases fall into two broad groups, those limited to an area in which cures by radiation are possible, and those which have invaded other structures in the pelvis and in which only temporary or palliative results may be expected. One can never know just how far the tissues are invaded, so a radiation dose sufficient quickly to destroy all the cancer cells in the field thought to be involved, must be used. Unscreened radium is never permitted in any field where there is danger of invading healthy mucous membranes. The author uses fifty to one hundred milligrams for each application, filtered with the usual 0.5 millimeter of silver, one millimeter of brass and one or two millimeters of rubber. Three thousand milligram hours, which is about the minimum efficient amount, is usually sufficient thoroughly to sterilize a given limited cancer field under such screening. Radiation to be effective in these cases has to be used to the limit of toleration of whatever normal tissues may exist in this environment. In all cases where the cancer is thought to be localized, radium is considered all that is necessary. When there is doubt about this point and in patients where the cancer has reached the adnexa and extended or infiltrated beyond the cervix, short wave roentgen rays are used to the saturation point.

J. D. Camp, M.D.

The Treatment of Inoperable Cancer of the Pelvis by Radium. Albert Soiland. Am. Jour. Roentgenol. and Rad. Ther., Oct., 1924, p. 378.

THE EFFECTS OF X-RAY AND RADIUM THERAPY UPON TISSUES[1]

By H. R. WAHL, M.D., Kansas City, Kansas

THE average physician does not realize the antagonism that exists between the practical application and the scientific study of a new invention or discovery as soon as it bears a therapeutic aspect. Especially is this true if a remedy is suggested for a condition for which there is no satisfactory treatment, such as cancer. There is little patience with the slow, painstaking, but accurate methods of science, and what scientific basis is established, is soon submerged by the pressure of therapeutic necessity and commercial exploitation. This is particularly true of the discovery and development of the X-ray and radium, both of which suffer from the fact that their physical researches greatly out-distance their biological investigation. There is no doubt of their remarkable effects on living tissues, but so little is known of the basis for their action and so meager and conflicting are some of the studies on their effects, compared with the far-reaching applications that have been made, that a careful analysis of their real effects on tissues and cells is imperative, and fundamental studies of their biological action must be made and confirmed if a safe and conservative estimate is to be available, and glowing and spectacular accounts appropriately discounted.

There is much difference of opinion even among careful investigators regarding the way in which the effect of radium or the X-ray is produced. Some maintain that the action is directly on the cell itself, affecting the chromatin material in the nucleus, liberating its autolytic ferments or interfering with intracellular equilibrium. Others claim that the action is, first, upon supersensitive capillaries, resulting in their obliteration and the subsequent malnutrition of the part exposed. Still other investigators produce convincing evidence that the action is an indirect one and is due to an increase in the production of protective substances by surrounding healthy tissues. For a long time the theory of "direct action" was supported; then, a few years ago, the idea of "vascular obliteration" became popular, but now the pendulum is apparently swinging towards the concept of indirect action on the cell through stimulation of protective or immunizing substances, and that the cancer cell is not killed by the direct action of the X-ray. It is probable that all three are factors, the relative importance of which varies in individual cases.

Whatever the basis for the action of the X-ray its effect shows great variation in different tissues. The recent application of high voltage X-ray therapy to deep-seated tumors and lesions has made a thorough knowledge of the effect on various tissues of vital importance. When such exposures are made it is evident that three groups of tissues are involved: first, the tumor or lesion; second, the tissues traversed by the rays in reaching the tumor, and third, the circulating blood. When treatment is prolonged it is evident that the entire volume of circulating blood is exposed.

With the usual therapeutic dose the blood apparently is not greatly affected. The lymphoid cell is most susceptible, and a reduction may be produced in the blood. Lymphoid cells generally are easily destroyed, and, for this reason, pathological conditions such as Hodgkin's disease and lymphosarcoma rapidly melt away following radiation. There is some question as to whether this susceptibility of lymphoid tissue is not a contra-indication to radiotherapy of tumors, especially if MacCarty's work toward proving that the lymphoid cell is important in maintaining the bodily resistance to cancer is correct.

The skin is more resistant and has a long latent period. Some individuals are pecu-

[1]Read at the Tenth Annual Meeting of the Radiological Society of North America, Kansas City Missouri, December 9, 1924.

liarly sensitive and have incurred embarrassing delayed burns and ulcers weeks after receiving but a moderate dose. Striated muscle shows degeneration and even necrosis when in line of intensive treatment. The pancreas and heart show little effect. A radium or X-ray nephritis has been described, but is denied by Whipple and others. Secreting glands, such as the salivary glands, show no reaction with moderate doses, but with large therapeutic doses they undergo considerable degeneration, with subsequent lymphoid infiltration and fibrosis.

Warthin has recently described striking focal inflammatory lesions involving the bile ducts, particularly in patients who had received heavy deep X-ray therapy for deep-seated malignancies. The so-called X-ray sickness is said to be of hepatic origin.

The germinal epithelium has been known to be especially susceptible to the X-ray, repeated cases of sterility following X-ray therapy for uterine cancer, especially in the early days when the technic was not so well established. Much of the earlier work showing the inhibiting and destructive action of these actinic rays was carried on with a study of their effect on germinal cells.

One of the most susceptible tissues of the body is the epithelium of the small intestine. Whipple and his co-workers have shown this to be even less resistant than the lymphoid tissue of the intestinal tract. It was seriously damaged with moderate doses of deep X-ray therapy. There was considerable desquamation of the surface epithelium and degenerative changes in the crypts of the glands. These authors believe that the intestinal lesions cause a toxemia similar to the proteose intoxication, or to that which occurs in high intestinal obstruction, and they are emphatic in their belief that the radium and X-ray toxemia frequently reported with large doses is really due to injury to the intestinal epithelium. This we observed in one of our cases. They do not consider this a contra-indication to the use of deep therapy in lower abdominal lesions, but they feel that this is a potential danger to be avoided if possible and every known precaution used.

The action on the ductless glands is not well established. It causes an atrophy of the thymus gland, and is said to reduce thyroid tumors and to be of value in goiter, but this is subject to question except in isolated cases. Holfelder and Peiper have recently shown that the adrenal gland is twice as sensitive as the intestinal epithelium and that the adrenals show marked degenerative changes, especially in the cortex. They emphasize the danger of injuring the adrenal. They explain the roentgen malaise following gastric irradiation as due to transitory injury of the suprarenal capsule. Edema and hemorrhage have also been described in these organs.

Hoffman recently stated that 25 per cent of the skin erythema dose inhibits the growth of bone tissue and that a limb exposed to the X-ray shows retarded growth as compared to the untreated limb. He noted a retardation of the process of calcification.

The recent work of Davis shows the production of marked pleural thickenings and pulmonary fibroses following prolonged exposures of the chest, and conveys a warning against the danger of over-exposure of the chest in deep therapy, especially for malignancy of the breast.

The effect of the X-ray and radium upon tumors affords its greatest therapeutic application, but the cellular changes produced have not been thoroughly studied and our knowledge of their nature is very meager. The changes in tumor tissue after radiation are variable, depending upon the amount of exposure to the X-ray, the size and nature of the tumor and the susceptibility of the individual. These changes are so variable in different tumors that it is impossible to do more in a short paper than to indicate in a general way their character, using a

specific type of tumor and the effect of one large exposure.

The cells of a squamous carcinoma pass through five successive phases before their ultimate disappearance. First, the latent phase, varying from four to fifteen days, during which no cytological changes in the tumor cells may be noted. There may, however, be some inflammatory reaction in the stroma, usually nothing but hyperemia, some hemorrhage and beginning exudation of lymphocytes and polynuclear leukocytes.

The second phase is the development of monstrous characters in the cell. All parts of the cell may be enlarged. Often the cells are loosened and fuse together into multinucleated giant cells. Nuclear changes are particularly prominent. Many of the nuclei have become swollen, homogeneous in structure and hyperchromatic. A few may become pyknotic, and disintegrate. Mitotic figures are often very atypical and are usually infrequent. Many cells contain bodies having a pseudo-parasitic character. Leukocytic infiltration, especially of lymphoid cells, is often well marked. This phase usually develops in the second and third weeks.

The third phase is that of keratinization, which is followed by that of disintegration and phagocytosis. The tumor cells begin to degenerate and disappear, their disintegration seeming to be caused by polynuclear leukocytes, lymphoid cells and fibroblasts, which are unusually active. This change is often noted by the end of the third week after a large exposure. The tumor cells are soon reduced in number and often occur in small nests here and there, separated by increasing masses of stroma. Macrophages and plasma cells often accumulate about the vessels, remaining long after the disappearance of the tumor cells. Irregular keratinized masses may be seen about the periphery. Masses of degenerated cells may persist, cease to give specific reactions for keratin, and remain encapsulated for prolonged periods. After four or five weeks pyknotic nuclear fragments and occasional granules of agglutinated masses of chromatin may be all that is left of the tumor tissue.

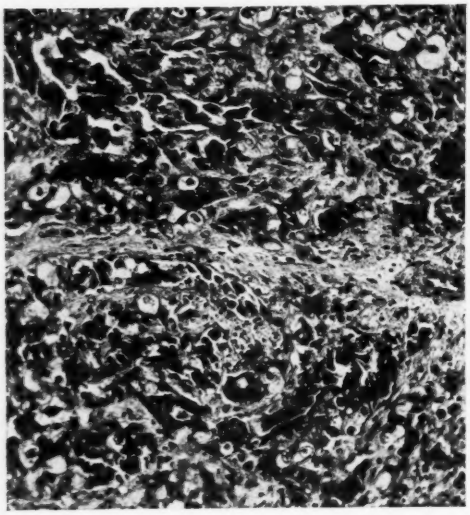

Fig. 1. Carcinoma of the upper jaw treated with radium needles 24 days before this specimen was removed. Note the hyperchromatic nuclei and the tendency of the cells to fuse together. Magn. 125 ×.

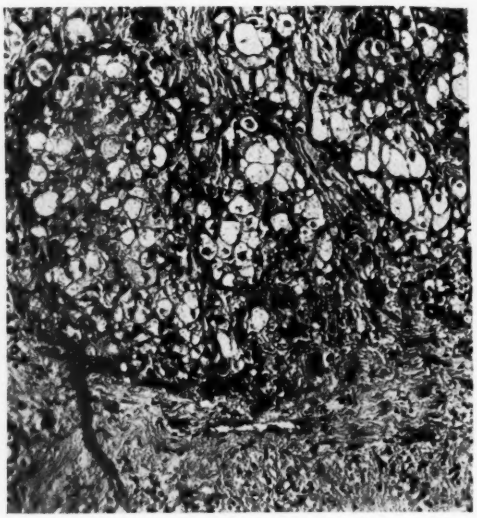

Fig. 2. Photomicrograph of the same case as shown in Figure 1, six weeks after treatment and two exposures to radium needles. Note the hyperchromatic nuclei and marked vacuolar change in the cytoplasm of the cells. Magn. 125 ×.

The last phase is the formation of scar tissue. The stroma usually shows considerable activity, the leukocytes are abundant and capillaries and fibroblasts proliferate, leading eventually to a peculiar cellular type of granulation tissue replacing the tumor tissue. An obliterating angitis is often described, especially with excessive exposures, but is not a constant finding. If the dosage has been exactly adjusted, the healing occurs without excessive scarring. If the dosage is too great, the vessels are destroyed. The stimulating action of the proliferating fibroblasts, capillaries and endothelial cells occurring with the correct dosage is absent and dense hyaline scar tissue results, such that neither leukocytes, vessels nor tumor cells can penetrate it. If the epidermis has not formed over, it may fail to do so because of lack of nutrition beneath, leaving a sluggish, non-healing ulcer. In this case refractory tumor cells may still exist, especially in the deeper portion, and are not exposed to resistant action of normal healthy tissue and become free to proliferate and often do so in spite of the presence of dense cicatricial fibrous tissue. In some cases the development of capillaries and fibroblasts becomes abnormal, so that large irregular blood spaces are formed, giving a telangiectatic appearance. This is especially the case where only the surface portion of the tumor has been exposed to radium or X-rays.

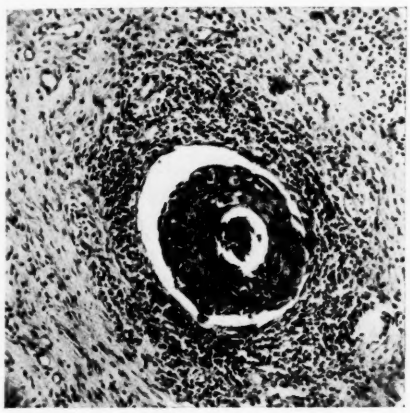

Fig. 3. Tumor metastasis in a lymph vessel from case of carcinoma of cervix which had been thoroughly treated with X-ray and radium for past seven weeks. The tumor had apparently disappeared but uterus was removed because of persistent pelvic tenderness. This area found in course of examination of uterus. Note mitotic figures in cells. Magn. 90 ×.

Fig. 4. Basal-cell epithelioma of face after combined X-ray and radium treatment for two months, leaving persistent non-healing indurated ulcer showing cords of degenerated tumor cells in the wall, as in this slide. Recurrence developed in glands of neck nine months later. Magn. 70 ×.

The basis of X-ray therapy of tumors has been that tumor tissue is more susceptible and more easily destroyed than normal tissues. There is some question as to the truth of this, it not having received universal acceptance. The X-ray is said to affect young cells, particularly cells in process of division, but it is recognized that all young cells in process of division are less resistant to physical agents, such as heat, than adult cells. The fact that those tumors which are most embryonic in character are most amenable to X-ray treatment does not justify the theory of a selective action on the part of the rays. It is more likely that the increased stimulation of the protective mechanism of the normal tissues, with decreased resistance of immature cells, is the essential factor in the destruction of the tumor cells.

The changes in tissues following radiation present the greatest range of variation, depending upon the exposure or dosage, the nature of the lesion and the individual. Too

large a dose may be as harmful as too short an exposure. This is particularly true of malignant tumors. Even with nicely adjusted dosages failure to eradicate a malignant tumor may occur. This is particularly true of the malignant tumors composed of considerable differentiated tissue, such as squamous-cell epithelioma of the tongue, adenocarcinoma of the stomach, and melanosarcoma. The natural history of these malignant growths should always make the prognosis of any form of therapy conservative. Two tumors of the same histological structure may react quite differently to the same X-ray dose. Even cells in different parts of the same tumor vary in their susceptibility to the X-ray. Just as there is marked variation in histological appearance in different tumors—and even in the same malignant tumor—so are there similar variations of X-ray susceptibility and resistance to the X-ray. Hence, certain tumor cells may survive the exposure and develop a new strain of cells resistant to radiation, regardless of its amount, and lead to progressive growth of the tumor in spite of continued radiation. This is nothing but an illustration of a general biological phenomenon in which a chemical or physical agent acts on masses of living organisms or cells. The same process results in the so-called salvarsan-fast spirochetes in some cases of syphilis. Schwarz noted a difference in the behavior of benign and malignant tumors to repeated doses of X-ray or radium, the former showing increasing susceptibility to the rays while the latter manifests a progressive increase in resistance.

If the present trend of scientific opinion, that the effect of the X-ray is not so much a direct as an indirect one, becomes generally accepted, the danger of overtreating a malignant growth becomes increasingly apparent, inasmuch as that treatment may lower some of the natural defenses of the body to the tumor growth, defenses which would be sufficient to overcome the few cells that have escaped the direct action of the rays.

It is probable that in X-ray therapy two cellular reactions occur, one which is nonspecific but destructive, acting on the young cells of a tumor, and the other which has a specific stimulating action due to multiplication of the natural body defenses, which indirectly act on cells that have resisted the direct action of the X-ray. This emphasizes the great weakness of X-ray and radium—the difficulty in ascertaining the correct dosage and applying it where needed. To secure the maximum effect the dose must not be too large or too small. The proper dosage varies with each individual case. There is no such thing as a fixed dose for a carcinoma, one for a sarcoma, etc. In determining the correct dosage the roentgenologist must deal with four factors, only one of which is stable, while the other three are biological variants. He is sure only of his X-ray technic. The biological variants are the individual patient, the nature of the tumor, and its location. The only way in which he can be sure of the nature of the tumor is by examination of a biopsy specimen, yet it is very rare that this is done. The roentgenologist has a tremendous responsibility, greater than that of the surgeon, and his judgment has less tangible tools with which to work. He must treat each individual case by itself. He has but two tangible tools; one is his X-ray machine, the other is an histological examination of the tissue to be destroyed. Yet the average man merely guesses at the nature of the growth, instead of studying it. How a man can treat a patient without certain knowledge of the nature of the lesion is inexplicable. The roentgenologist must know the anatomic relations, the histologic structure and biologic type of the growth, its duration, mode of extension and possible secondary complications, as well as the physical condition of the patient, before he can intelligently use the X-ray and radium and do justice to both his patient and to radiotherapy. Until a more thorough knowledge of the natural history of the tumors treated is associated with X-ray treatment than has been the case in the past,

I do not believe we can determine just when X-ray therapy is indicated and when not.

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Cervical ribs in children.—The writers report 13 cases of cervical ribs occurring in children, varying in age from 4 to 12 years. Such ribs may be found in children at all ages. Todd believes that symptoms in many cases are often delayed until the descent of the shoulder girdle, which is not complete till the third decade of life. Stopford thinks that a weakness of the supporting muscles, producing a dropping of the shoulder girdle, thus producing a stretching of the nerve trunks over the rib, may also be an additional factor. The authors suggest as a further explanation that ossification is not complete till after adolescence, and that the increase in growth and size of the rib may lead to greater pressure on the nerve trunks.

Occasionally these ribs may give rise to definite symptoms in young children, similar to the symptoms seen in adults. Where symptoms are present, a short course of non-operative treatment to promote development of the muscles supporting the shoulder girdle should be tried. If no improvement is noted in two or three weeks, surgical removal of these ribs is indicated.

Solomon Fineman, M.D.

Cervical Ribs in Children. A. H. Southam and W. J. S. Bythell. Brit. Med. Jour., Nov. 8, 1924, p. 844.

Dye for gall-bladder and biliary tract function test.—Methylene blue, indigocarmin, neutral red, phenolsulphonephthalein and phenoltetrachlorphthalein, which are now used for the liver function test, are not suitable dyes for that purpose. As azorubin S (A) is harmless and stable and appears in the bile in a very high concentration, this dye is one of the most suitable for the liver function test made by means of the duodenal tube. The small amount excreted in the urine can be utilized for the indirect measurement of the liver disturbance, as the excreting condition in the urine increases very markedly. Five minutes after the injection of the dye, magnesium sulphate is given. The duodenal content is stained in seventeen minutes, which is the time of the first appearance of the dye in the normal subject. The staining reaction is very distinct and clear. When this dye is applied in the gall-bladder and biliary tract function test, it is a very easy and simple matter to obtain an infallible result. After the instillation of the magnesium sulphate solution, the bile obtained is the content of the gall bladder.

W. W. Wasson, M.D.

A New Dye for Test of Liver and Biliary Tract Function. Yoshinori Tada and Kokichi Nakashima. Jour. A. M. A., Oct. 25, 1924, p. 1292.

THE DIFFICULTY OF DIAGNOSIS OF CARCINOMA OF THE BREAST[1]

By MALVERN B. CLOPTON, M.D., St. Louis, Missouri

AS we are to discuss the difficulty of diagnosis of carcinoma of the breast, we can leave out of consideration those cases where the findings are all too plain, showing the classical picture of adherent skin, retracted nipple, fixation of pectoral fascia, extensive axillary involvement. Such findings leave us no room for doubt, but the patient may still have a chance for relief, if nothing else, by a judicious operation and sufficient radiation. If we find a deep involvement of the chest wall, extensive skin metastasis and enlarged and fixed axillary and cervical lymph nodes, secondary growths in the lungs, liver or other viscera, or in bone, we are dealing with a hopeless case of cancer, which should not be operated upon, but may be greatly relieved by X-ray.

Having thus put out of the question the unmistakable case, we are left to deal with the case which may or may not be cancer, and which does not conform in any unquestionable way with the classical picture of cancer.

Before taking up the individual signs and symptoms, we may consider for a moment the likelihood of our diagnosis being correct. In the light of the experience of one large clinic (1) where their diagnoses have been checked by their pathologist, who reviewed over 2,100 histories, it was found that in only 80 per cent were the clinicians willing to make a positive diagnosis before operation, and that when they expressed a positive diagnosis of cancer they were correct in 95 per cent of the cases.[2] The clinicians were able to make correct positive diagnosis of a benign condition of the breast in about eight out of ten cases. This leaves a group of cases in which the most experienced men are likely to go wrong, as they afford the greatest difficulties in diagnosis.

What are the chances of a tumor of the breast being benign or malignant? The older surgeons were accustomed to say that at least 80 per cent of all mammary neoplasms were carcinomatous. But in recent years, under the stimulus of the agencies trying to prevent the ravages of cancer, there are more women coming to doctors for a lump in the breast, because they have been told that many benign tumors are potentially malignant, and that the hope of cure is to take out the growth before it becomes cancer, or to remove the cancer early.

The more recent statistics (2) show that in 334 cases of tumor of the breast, 136 (41 per cent) were benign and 195 (59 per cent) were malignant. One would infer from MacCarty's (1) statistics that the proportion of benign growths is about what was stated by the older surgeons, and in his studies it is interesting to note that carcinoma was not diagnosed positively before operation by the clinician in 245 out of 2,100 cases. With the ever-present fear of cancer which is inherent in every woman's mind, more doubtful cases are coming for consultation, and since the likelihood of making a correct diagnosis in the beginning is much less than in the more developed state, we feel that it is necessary to clear the diagnosis in many cases by an incision or excision of the growth. The surgeon should be trained to make the diagnosis from the gross specimen, which he can do in the greater proportion of cases, but there may be a small percentage where only the microscopic picture will decide. When dividing the growth one must note the resistance to the incision (Is it hard or soft?), the appearance of the surface of the growth (Is it regularly or irregularly marked?), if it cups on section, if there is much cell juice, and, further, how the tumor grows and what is its relation to the surrounding tissue,—whether it invades or is

[1] Read before the Radiological Society of North America, at Kansas City, December, 1924.

[2] In these cases are included all grades of carcinomatous involvement, of which only 50 per cent were operable.

encapsulated. The microscopic picture and the type of growth may help in subsequent classifications, but the point that should determine the operative procedure is the method of growth of the tumor, and, in case of doubt, it is better to excise the breast and fascias and adjacent lymphatics, on the suspicion of an organ being potentially, if not actually, cancerous, than to allow the chance of cure to pass. Nor is it always wise to await the pathologist's report to decide the question of malignancy. He may select a portion of the growth that, when studied, does not impress him as invasive, and his opinion may be couched in terms that are hard to interpret. What person but is bewildered when the long list of pathologic terms is laid before him, and who will decide what classification is to be used, when all our leading pathologists seem to differ among themselves? For the surgeon must bear in mind that epithelial and fibrous tissue elements are blended in all growths, with one or the other predominating. There may be long-standing growths, made up almost wholly of epithelium, that are benign, but they may eventually show cancer, or there may be growths made up mostly of fibrous tissue elements that remain as such for a long time, but they always contain epithelial elements and may become carcinoma. They rarely, if ever, become sarcomatous, but when they do they belong to the class known as adenosarcoma, a later stage of intracanalicular myxoma. One striking observation is that the breast is surprisingly immune from pure sarcomatous affections.

Between the varieties of epithelial malignant growths one cannot draw hard and fast lines, and the rough grouping into adenocarcinoma, medullary carcinoma and scirrhous carcinoma does not clear the subject to any great extent, except that this classification helps to indicate the malignancy in a feeble way.

The origin of adenocarcinoma is chiefly in cysts of the involutional breast or in cystic adenomas, and they may, and most often do, run a very benign course, but they can be rapidly malignant. Distinctly fibrous carcinomas are, as a rule, less malignant than the more cellular forms, but their clinical course varies greatly. Medullary or encephaloid tumors are bulky, soft and cellular, and usually follow a very malignant course, with an early invasion of the skin through which they may ulcerate. They attack the lymph nodes and muscles early, and are extensively disseminated.

These fully developed cancers offer interesting problems to the pathologists, which I am neither able nor willing to discuss. The points that I want to dwell on are some of the clinical signs and symptoms, which help in the diagnosis, and later to discuss some conditions of the breast that behave as benign lesions but may develop malignancy. These are for our purposes not the least important lesions, as our hope of future improvement in our results of treatment must in large part rest on our ability to spot the pre-cancerous lesion and eradicate it. But I do not want the statement about benign growths transforming into malignant growths to be interpreted to mean that cancers always develop in this way. Most cancers begin as such, and are never anything else.

In taking the history we find patients placing emphasis on the hereditary features, if they are present, and we are inclined to think, inasmuch as our statistics show only from 5 to 24 per cent of cancers in the family, that this may be a negligible factor, but if Maud Slye's studies on experimental animals can be taken as analogous to man, the feature of heredity is not to be disregarded.

The patient is also inclined to attach much significance to bleeding from the nipple. The most common causes for bleeding from the nipple are the benign papillomatous proliferations of the duct linings, and according to Greenough and Simmons (3), a serous or bloody discharge is of the greatest value in differentiating papillary from other tumors of the breast. This discharge was present in eleven of their twenty cases. Dickinson (4) points to the fact that fibroid

tumors may cause sufficient irritation in the breast of those who have not reached the menopause to occasionally cause bleeding from the nipple at the menstrual period. Hald (5) has found bleeding in from only 1 to 9 per cent of malignant breast tumors.

The important information to be gained from the patient is the time when the tumor was first noticed, what it felt like, what has been its subsequent course, and what change in size or shape and when the axillary or other nodes were first made out. Pain is not in any degree indicative of malignancy.

The appearance of the breast may reveal many important things. Comparing the size of the two glands, one may recognize the contracture that comes with a deeply embedded growth, or the enlargement, either diffuse or localized, that comes with a myxofibroma, or the bulging of an adenoma. Adenoma, as well as cancer, may ulcerate the overlying skin. The nipple may be displaced on the breast, either because of the enlargement of one side from a benign growth, or the contraction of the other side by a cicatrizing malignancy. The nipple may be retracted, which is usually regarded as a sign of malignancy, but it is also encountered in adenomas taking their origin in the ducts. The enlargement of the superficial blood vessels has often been regarded as an evidence of malignancy, but it may accompany the chronic mastitis or a large tumor, such as a fibromyxoma. The excursion of both breasts over the chest wall is to be studied, and any limitation may give a clue to a deep-seated contraction about a tumor not either seen or easily palpated. At the same time one can get the first suggestion of a change in the skin due to contraction of the fascial bundles, that, if it progresses further, would lead to the "pig skin" or "orange peel" appearance.

Palpation of the breasts is the next step in the examination and should be made with the patient sitting. The observer should be behind and the hands should cover both breasts. In this way the smallest irregularities can be made out, because of pressure of the mass against the chest wall. The "feel" of the tumor is the criterion for most of the surgeons in making a decision for or against malignancy, but bear in mind that a tense cyst, an adenofibroma and a cancer may be of equal hardness. The movability of the lump through the breast tissue will help to decide the issue, but a cyst in an involution breast may often have a slight excursion and many times feel as irregular in outline as a cancer, and at times one encounters a small adenocarcinoma that is as smooth as an onion and slips about in the breast tissue without apparent restraint.

Bear in mind that cancers often have their origin in aberrant breast tissue, particularly along the upper part of the axillary margin of the pectoralis major.

Lymph nodes in the axilla are always suspicious signs of a malignancy in the nodule felt in the breast. But enlarged glands, even in the presence of cancer in the breast, are not necessarily metastatic, and simple benign tumors or cysts are not infrequently accompanied by palpable glands. Axillary nodes, even of large size, are at times the first evidence of a malignant growth in the breast, and we have seen such a case where the parent growth was not found until the whole breast had been sliced into thin layers, when a pea-sized cancer was discovered in a mamma much altered by chronic mastitis.

Let us now consider some of the benign conditions seen in breasts that offer opportunities for malignant changes.

The most frequent benign condition that brings a woman for consultation is the abnormal involution change known by many names, but most commonly called chronic cystic mastitis, which occurs at the cancer age and is more frequently seen in breasts that have never been the seat of lacteal hypertrophy. The clinical picture is not always easy to recognize. The onset is slow and usually painless, but at times the pain is so intense, particularly at the time when menstruation should have occurred, that this symptom alone may call for removal of the gland. Often the disease is so free

from symptoms that it is not recognized until a cyst of some size attracts attention. Bloodgood has separated the disease roughly into two groups. The first may be called the cystic, in which one finds in one or both breasts one or more smooth-walled cysts. In this type carcinoma is rarely observed, and excision of the cyst wall is usually sufficient. In the second type large cysts are not present, the disease consists of a localized enlargement of part of one or both breasts, due to a parenchymatous hypertrophy, called adenocystic, and this is what has often been considered a new-growth. In this form carcinoma is so frequent that removal of the breast or breasts is recommended in every case. Speese (6) found carcinoma developing in 26 per cent of the cases of cystic mastitis that he studied, and in 295 cases, collected from all sources, cancer was shown in 15 per cent. In the majority of early cases there are no signs by which a malignant degeneration can be diagnosed. Enlargement of the axillary nodes, slight inversion of the nipple, induration of the tumor, pain and tenderness, rapid growth, and discharge from the nipple are all symptoms seen in non-malignant cases. The diagnosis of early malignancy will have to be made in the majority of instances at the time of operation, when incision into the suspected area may disclose carcinoma.

A very common tumor, appearing especially in younger women, is the solid encapsulated fibroma, which is freely movable in the breast. Its slow growth marks little change from month to month, but occasionally it grows progressively larger, and in former times would sometimes be seen of great size. It is rare now to see this rapidly growing benign tumor of large size, as few are permitted to develop without operation. As encountered early, they are small and circumscribed, but there is evidence enough that they may become malignant in a fair proportion, when carcinoma develops. In a recent case of mine the patient for three years had noticed the smooth movable tumor, but in the last three months a secondary nodule developed, superficial to the fibroma, at a time when pregnancy began, and this was cancer. Speese reports a similar case. Ewing (7) says, "Adenosarcoma of the breast is very rare and usually follows a longstanding adenoma." Probably the rarity of this type of growth at present is due to the early removal of most adenofibromas. Many such tumors that have undergone myxomatous change are erroneously considered myxosarcoma. The pure sarcoma of the breast is rarely seen.

The other class of benign fibroepithelial tumors is one in which the epithelial growth overshadows the fibrous, and is divided into two groups: first, fibrocystadenomas, which are very rare; second,—a group which is not uncommon,—the papillary cyst adenomas,—localized tumors that involve as a rule the large ducts of the breast. They consist of one or more cysts partially filled with papillary outgrowths arising from the wall. As Greenough and Simmons (3) say, the symptoms are perhaps more characteristic and better defined than of any other tumors of the breast. One or more nodules are found in the center of the breast, not far from the nipple, hard, and, if not too deep in the breast tissue, may gave an elastic or cystic feel. Pain is present in about half the cases, but not severe and not a conspicuous symptom, as in cystic mastitis. There is a serous or bloody discharge in most of the cases. The tumors grow slowly. In three of the 20 cases reported by Greenough and Simmons (3), carcinoma was present in the wall of the cyst, and all were adenocarcinomas, of a low type of malignancy, and all made the nipple retract.

Paget's disease, which presumably starts in the ducts of the breast, and later shows the eczematous condition about the nipple and skin which makes its appearance characteristic, should be regarded as carcinoma and be treated radically.

Dr. Lee (8) called attention to a number of cases of fat necrosis of the breast which simulated cancer, occurring in fat patients with large breasts. The chief diagnostic

aid is the history of trauma, in three out of five cases due to hypodermoclysis. The tumor was hard, the overlying skin fixed, and there were lymph nodes in the axilla in one case. This is one form of inflammation that makes diagnosis difficult, and the cut section, as in other inflammations, may give the surgeon a problem that cannot be solved at the operation without a microscopic study.

I have dwelt in a sketchy way on the various types of lesions to bring out the fact that all benign growths have a certain malignant potentiality. I have pointed out that early cancer cannot be diagnosed by palpation or inspection.

I want to emphasize that all mammary growths should be considered malignant until proved innocent. It is therefore necessary, unless the malignancy is obvious, to operate on every breast tumor in a woman of the cancer-bearing age, and by inspection or microscopical examination determine the nature of the growth. The only hope of making our breast cancer statistics better is to do a radical operation earlier. X-ray may prolong life after a recurrence, or delay the appearance of recurrences. It cannot cure. Nothing but early operation will do that.

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8. Lee: Surg., Gynec. and Obst., 1921, XXXIV, 521.

Carcinoma of uterus.—The authors have used 10 to 12½ milligram needles, placing about six in the cervix around the growth, and 50 milligrams in the cervical canal. When possible this is left in place for twenty-four hours and the patient instructed to return in four weeks for examination. If the reaction is at an end at this time another application is made, and the patient observed four weeks later. If extension of the growth is noted at this time, further radiation is useless, the authors believe, as they have seen no case benefited that shows such an early recurrence. Two hundred nineteen cases have been treated with this technic, but not more than ten are alive and free from symptoms.

The authors have seen no evidence in their patients of anything resembling a real cure or complete disappearance of the pathological process. An arrest of the progress of the disease, a more or less lasting dormancy of the condition, is all that they hope for, and for this reason urge surgical removal of the early focus wherever possible. In the treatment of carcinoma of the uterus, as in all other regions, in those cases where surgery offers something definite, radium should be used secondarily or preoperatively, and the primary use of radium reserved for those definitely inoperable cases where the only real outlook is palliation.

J. D. Camp, M.D.

Radiation in the Treatment of Carcinoma of the Uterus. E. C. Samuel and E. R. Bowie. Am. Jour. Roentgenol. and Rad. Ther., Oct., 1924, p. 370.

RESULTS OF RADIOLOGICAL TREATMENT OF CARCINOMA OF THE BREAST[1]

By JOHN F. McCULLOUGH, M.D., PITTSBURGH, PENN.

THE advances in radiotherapy in recent years have caused physicians the world over to focus more attention upon the benefits to be derived from treatment by X-rays and radium. The recent furor created by the advent of high voltage radiation has attracted, more than ever before, the attention of medical men to the use of radiation therapy in the treatment of malignancy.

In the battle against malignancy of the breast to-day, surgery has established itself as capable of producing certain definite results. Surgeons admit that further improvement in technic is unlooked for and that the limits to which surgery can go have been reached.

Ever since it was apparent that cancer cells are apt to be located in areas beyond the limits accessible to surgery, there has been a demand for some method to supplement surgery in the treatment of carcinoma. Thus far the only recognized method employed in conjunction with surgery in breast carcinoma is the use of X-rays and radium. There has been abundant clinical evidence, together with much experimental data, to establish as an effective measure X-ray and radium therapy in the treatment of malignancy. Radiation therapy is an accepted institution in the treatment of carcinoma to-day. That surgery and radiotherapy represent the sum total of the methods we possess in combating carcinoma of the breast is admitted by everyone.

Halstead is quoted as stating, "Notwithstanding the present-day operation, death occurred from metastasis in 23.4 per cent of cases where the axilla was microscopically negative."

Greenough states that, "When the axillary glands are palpably involved only 12 per cent are cured by operation alone," but he adds, "with proper raying this may be increased to 20 per cent."

A number of writers quote Finsterer as stating that when the axillary glands are involved the number of cures by surgery alone is 4.3 per cent. Ewing believes that this represents about the average surgical success under these conditions. It is apparent, then, that a woman has one chance in twenty-five of being cured by operation, if she has a mammary carcinoma with palpable involvement of the axillary glands.

It is claimed by radiologists that in breast carcinoma radiation intelligently combined with surgery in the form of pre-operative raying, followed by surgery, and finally post-operative radiation offers a better outlook than surgery alone. The problem confronting those dealing with mammary carcinoma at the present time is to obtain a true evaluation of radiation as applied in breast carcinoma and to find a way for the proper co-ordination of both methods of treatment.

When one views the radiotherapy situation as applied in treatment of cancer of the breast, it is at once apparent that in a large percentage of cases the use of X-ray and radium supplants surgery. The group of cases to which this applies is composed of those in which, by reason of extensive involvement or because of recurrence or metastasis, nothing but increased misery and a more hasty demise could be looked for if subjected to surgery. Surgeons have recognized ever since the peculiar susceptibility of neoplastic tissues to radiation was demonstrated that this form of treatment should be the method of choice in inoperable, recurrent, and metastatic cases. While there is ample reason for skepticism as to the curative value of radiation in such cases, surgeons and radiologists agree as to the palliation value. Clinical experience has

[1]Read before the Radiological Society of North America, at Kansas City, December, 1924.

proven, in apparently hopeless cases, that much suffering has been prevented and that many cases living in misery have been brought to a state of comparative comfort by the use of radiotherapy. Life has been prolonged over various periods of time, ranging from one to five, and in a few cases to ten or more years.

The results to be obtained when radiation is employed in inoperable cases depend very much upon many factors: the nature and extent of involvement and the amount of dissemination; the age and condition of the patient; the degree of anemia and cachexia present and the state of nutrition. After all these conditions are considered, the choice of the agent to be employed and its method of employment have been found to have some bearing upon the results.

It is generally acknowledged that the primary inoperable tumor has usually reached a stage of extensive infiltration, and it has been found also at this stage that varied types of carcinoma may be found in different sections of the same tumor. Fibrocarcinomatous elements may be found in one section and cellular predominance in others. A diffuse, markedly cellular carcinoma in a young woman is less amenable to improvement than a hard fibrocarcinoma in an older woman. Fungating adenocarcinomas often melt very easily.

EXTENT OF INVOLVEMENT AND AMOUNT OF DISSEMINATION

Upon these two factors depends very largely whether or not a case is inoperable. So also upon these factors depends in a large measure the degree of success to be hoped for by radiotherapy. It is a generally accepted fact that only purely localized cancers give good results when treated surgically, yet the average surgeon seems to consider only well advanced cases inoperable, and it has been this advanced class of cases that has furnished a large part of the material upon which radiotherapy has shown good effects. Were a more rational selection made of cases considered inoperable, the benefits to be derived from radiotherapy might make a better showing, perhaps equal the results of surgery in certain cases. If surgery should be used on operable malignant growths, it is equally true that those which are inoperable should be treated by radiation. Meddlesome and partial surgery is worse than useless, and brings only discredit to a method which has achieved so much.

Surgery applied in inoperable cases makes more difficult the production of good results by radiation. Christie claims that 75 per cent of cases operated upon still have cancer and that this large group of cases are in worse condition than before subjected to surgery. Worse not only from the patient's standpoint, but worse from the standpoint of anticipated benefit from radiotherapy.

It is generally recognized that cancer of the breast, in the beginning, is a local disease, which remains localized for a comparatively short period. From this primary focus, there is early dissemination along the lymphatic channels and usually early involvement of the axillary lymph nodes. The most difficult problem to determine in the treatment of carcinoma of the breast is the extent to which dissemination might have already taken place.

Schmitz claims that whenever carcinoma is no longer a localized disease it belongs to radiotherapy. With marked involvement of axillary glands on the same side as the breast lesion, with extension well up under the clavicle, or with palpable supraclavicular nodes, the carcinoma is no longer localized. Fixation of the tumor to the chest wall is a frequent finding and should be considered indicative of the fact that the cancer is no longer localized. In these, by means of the usual operative procedures, complete removal of all of the carcinomatous tissue cannot be accomplished. In these cases the bulk of the tumor mass is removed, but the remaining portions are traumatized and stirred up to greater activity. In many, localization no longer exists, because of diffuse skin involvement.

Examination of the opposite breast frequently reveals evidence of metastatic involvement. Lee lays stress upon the frequency with which one can palpate axillary nodes in the opposite axilla.

Metastasis to bones, found even in cases with small tumors in the breast associated with little or no axillary glandular involvement, emphasizes the necessity for care to be exercised in running down symptoms such as pain in the back or hips, often diagnosed and treated as neuritis of focal infection origin, and found as it develops farther to be metastatic bone involvement. So also is important the early recognition of involvement within the chest.

CHOICE OF AGENT TO BE EMPLOYED AND ITS METHOD OF EMPLOYMENT

Those who were engaged in radiotherapy ten years ago had as their principal instrument of attack the old type gas tube. The difficulties encountered in the use of this apparatus are still fresh in the memory of many. It was impossible then to have the accuracy and exactness of control which is required to make more generally applicable the use of X-ray therapy in the treatment of malignancy. Through the cumulative character of the X-ray effect of doses repeated at intervals of from two to four weeks, good results were obtained, tumors were caused to shrink and recurrent masses to disappear. With the advent of the Coolidge tube there was presented a means of administering more accurate and more concentrated dosages on diseased parts. The administration of what was termed "lethal dosage" became the object sought.

Further efforts to administer lethal dosage, especially within the deeper tissues, have resulted in the more recent advance in radiotherapy, namely, the employment of high voltage apparatus. It has been stated that success in the employment of this more intense radiation seems to call for a sharper concentration in the involved area only, avoiding as much as possible strong radiation of adjacent and underlying tissue. The more the dose can be confined to cancerous parts only, the better will be the result. The topography of breast malignancy and the wide distribution of its metastatic dissemination make difficult the extreme accuracy and exactness necessary for success with high voltage radiotherapy.

At present sufficient data have not been collected, since the advent of high voltage radiation, to permit of its being advocated as generally applicable in all inoperable cases of breast carcinoma. Lee states that its field of usefulness seems to be limited to inoperable breast conditions associated with large masses, deep-seated metastasis, and large breasts with diffuse infiltration.

Associated with intense radiation has been the employment of massive dosage, and massive dosage has resulted in intoxication and serious tissue changes, which in some instances have been thought to have aggravated rather than improved the patient's condition.

Satisfactory regression has been accomplished for years by machines delivering up to 140 kilovolts. This, supplemented or combined with suitable radium therapy in the form of radium pack or radium in needles buried in the tissues, has resulted in such improvement in inoperable breast malignancies that it offers suitable argument for the employment of radiotherapy in all cases of breast malignancy. Surgeons and the profession in general offer no opposition to the claims that inoperable carcinoma of the breast belongs to the field of radiotherapy. There is, however, considerable difference in judgment as to what constitutes operable and inoperable carcinoma of the breast.

In 1922 Lee grouped certain factors, which, when found to be present, should place the case in the inoperable group. He found that 61.2 per cent of cases admitted to Memorial Hospital in 1920 were in the inoperable stage at the time of entering the hospital, according to his grouping. If all surgeons adhered more closely to the selection of operable cases as advocated by Dr. Lee, radiation therapy would be more gen-

erally employed, and the results in the treatment of breast cancer would show improvement. In support of this we need but refer to conclusions of Dr. Holmes, in 1921, as follows: "Recently we have had a small group of cases of carcinoma of the breast in which there was evidence of metastasis, glands being palpable in the axilla and above the clavicle. For this or other reasons, they were not operated on, but were subjected to X-ray treatment alone. These cases have certainly done much better than similar cases operated upon and followed by radiation. I cannot but feel that the operation in some way breaks down the natural resistance of the patient, and interferes with the walling off process which is the result of connective-tissue stimulation."

In discussing malignant growths of the breast some years ago, Hernaman-Johnson said: "Malignant growth in this region can often be made to disappear by X-rays alone, so far as inspection and casual palpation are concerned; but rarely to such an extent that remains cannot be detected when carefully sought for. Far more important is the fact, long suspected on clinical grounds, but recently—in the opinion of many competent to judge—experimentally proved, that X-rays in suitable doses raise the immunity of the body to cancerous invasion. Radiotherapy should therefore be administered before operative removal. Such preoperative treatment has the dual advantage of depressing cancer cells locally before any surgical trauma has disturbed them, and at the same time increasing the general powers of resistance to any subsequent migration."

He states further: "In view of what Sampson Handley has shown as to the radiating growth of cancer along the lymphatics, it is obvious that the local treatment should embrace a very wide area. The individual doses should be small and be repeated two or three times a week; it is possible to obtain a quick local effect at the expense of general resistance. From two to three weeks should be spent in this preparatory treatment."

Most radiologists recommend, and have done so for years, that radiation be given before operation. It will be found, however, that if inquiry is made of all patients sent for radiation after surgical removal of the breast as to whether the breast was treated by X-rays or radium before operation, the great majority will report in the negative. It would seem, therefore, that surgeons in general are ignoring very plausible benefits to which the breast cancer victim is entitled.

Groover, Christie and Merritt state that the most favorable time for operative interference in cancer of the breast is about six or eight weeks after instituting roentgen treatment. They advocate such a course, convinced that there will result certain advantages, as follows:

1. In practically all cases the surgeon will actually have less cancer tissue to remove. In many cases this will amount to 50 per cent.
2. Danger of local implants will be lessened.
3. The danger of cancer dissemination incident to handling of the tumor and traumatization of tissues will be restricted.
4. A considerable number of borderline cases will become definitely operable.

Observations of the effects of high voltage radiation have recently brought out some very interesting conclusions. In discussing the present status of high voltage radiation therapy of cancer, Herly quotes conclusions of a number of radiologists, practical application of which should be kept in mind when planning radiation previous to operative interference.

Perthes is quoted as concluding that, "The power of resistance of the entire organism plays as important a part as does the normal tissue immediately around the tumor cells. When these protective forces are diminished by too intensive and too extended raying, and when the roentgen cachexia, so-called by Kroenig, develops, then we observe, instead of the attempted cure of cancer, a striking proliferation of cancer cells. This is a distinct hint that in roentgen

therapy consideration of the general organism cannot be disregarded." Perthes believes the more intensive the raying the worse the results.

Levy-Dorn points out that "X-rays influence the cancer cells directly, though they do not kill them in the sense of a knock-out. To obtain this effect, something must be added. It probably results from the effect of the rays on the neighboring tissues and perhaps on the organism as a whole by increasing, in a manner not at present understood, the protective forces of the body. This is partly proved by the fact that you may ray one part of the body and have a newgrowth disappear in another unrayed part. Intensive raying will damage the connective tissue, which must be regarded as a barrier to the cancer cell, and injury to it opens a breach in the protective wall, allowing an invasion of the cancer cells that are left unaffected by the radiation."

Pilger, in a recent article on the "Erlangen Treatment of Malignant Diseases," ventures to say that improvement lies in the attainment of administering sharply concentrated massive doses strictly confined to the primary focus, with slighter radiation of the surrounding tissues. He is personally convinced of the improvement in this method by his experience in cancer of the tongue. He found that by reducing the area of intensive dose as far as possible to the primary focus of the cancer, giving there a dose of 120 to 130 per cent and treating the involved areas and their immediate surroundings as usual with 90 to 100 per cent, he brought about a remarkable chain of results which have become very good.

For years a number of radiologists have been recommending a somewhat similar procedure in breast carcinoma as a preoperative measure—surface radiation by X-rays or radium or both, followed by imbedding radium in the breast. By placing radium within the mass in the breast of operable cases, there is provided sharply concentrated massive doses, strictly confined to the primary focus, while the preliminary surface application provides slighter radiation for the surrounding tissues. It is claimed that by the preliminary surface radiation the lymphatics wide of the tumor mass may reasonably be considered sealed, and the sharply concentrated massive dose of radium has been thought to prevent cell proliferation and produce what Pfahler has termed "devitalization of the cancer cells," so as to interfere with their inoculation or further development.

A number of years ago, I had the privilege of using X-rays upon a number of breast carcinoma cases before the breasts were amputated. In few instances was sufficient time allowed to elapse for tissue changes to be noticeable. In fact, most cases were treated surgically within a few days after completion of the X-ray treatment. The fear of losing valuable time and thereby causing the patient to suffer has subjected surgeons in general to great anxiety in these cases, and has deterred most of them from awaiting the full benefits of radiation. By such a method quick local effects may be obtained, such as devitalization of the cancer cells by direct action of the radiation, and, in addition, the effect produced in the surrounding tissues by the action upon the lymphatics draining the affected area, but sight is lost of what Perthes terms the "power of resistance of the entire organism." This, he claims, plays as important a part as the normal tissues immediately around the tumor cells.

Within the last few years we have had opportunities to use radium by imbedding needles within the tumor mass after having previously given surface radiation by radium packs and X-rays, as advocated by the late Dr. Boggs. Our observations of the results of such treatment are in accord with the claims of Groover, Christie and Merritt in these cases.

If after the removal of a cancer growth no cancer tissue remains behind which could give rise to a new starting point, then the individual is perfectly cured; but in most instances all trace of the cancer growth is not removed, some residue being left behind which sooner or later continues

to grow and gives rise to recurrences and a metastatic process. To prevent recurrence and spread of the disease, radiation after operation has for years been urged.

Pfahler states that "It has been shown that radiation effects are most evident on new growing tumor, and such radiation will prevent the growth of inoculated tumors. Therefore, active post-operative treatment should be given in cancer of the breast." He claims that "the object of the post-operative treatment is further to devitalize remaining cancer cells which have escaped the surgeon's knife and to prevent the growth of newly implanted tumor."

We do not know to what extent cancer cells left behind have been devitalized and prevented from producing newgrowths, but, as Pfahler claims, under such conditions it is reasonable to believe that an increased number of cures should result.

Handley claims to have observed much benefit from this form of treatment. Herly quotes the results of Anschuetz in Kiel, who reports that of 230 cases of breast cancer post-operatively radiated with an old apparatus, 60 per cent had a more than five-year clinical cure, while of those not radiated prophylactically only 38 per cent had similar good results. These statistics were handled very carefully; the intercurrent deaths were all counted as recurrences; all doubtful cases were excluded from the statistics, and the specimens of all cases operated on were kept and again examined after five years to avoid any possible mistakes.

Post-operative radiation, while it has on the whole been discouraging so far as preventing recurrences from taking place, has in the hands of most radiologists been productive of sufficient palliation to make its use commendable. Clinical experience shows that in many instances recurrences of breast cancer respond less favorably to radiotherapy than do primary growths. In these cases the general bodily resistance to cancer invasion and the local tissue resistances have been interfered with by operation. I am sure surgeons and radiologists both have observed, following operation, rapid dissemination and metastasis, which can be attributed only to—as Holmes puts it—"break-down of natural resistance."

The stimulation and preservation of the defensive powers seem to be requisite for improvement in the results in treatment of malignancy. To this end Hirsch states that an examination of the dosage required to depress the vitality of the pathological tissues and to stimulate the defensive powers is important. He asks: "Is it not essential that we deliver the radiation with the intent and purpose of depressing the vitality of the cancer cell, and at the same time stimulating the reconstructive forces and powers of the body, local and general? This seems to be the problem confronting radiologists to-day."

The power of resistance of the entire organism must command more attention. Surgery should be applied at the most favorable time. This, we believe, is after careful and somewhat time-consuming radiation. The radiologist must avoid reducing this natural power of defense and must seek ways of increasing it. He must set himself to supplement Nature's efforts to repair.

DISCUSSION

DR. H. G. SCHMITZ (Chicago): The symposium has been very instructive. How shall we combine the opinions of pathologists, surgeons and radiologists so that our patients may benefit to the greatest possible extent? In the first place, we should recognize that the microscopic examination of excised tissue is essential for correct diagnosis and sound treatment. A carcinoma with little connective tissue is an acute growth and kills the patient very soon, while a cancer containing a large amount of connective tissue usually runs a more chronic course. In the examination of the patient we must observe four facts which immediately tell us the extent of the carcinoma, and, based on these four points, the cases can be grouped and the indicated treatment correctly applied. The facts elicited on physical examination are: (1) Is the carcinoma

clearly localized? By a localized carcinoma we mean a growth that is still small and has under no circumstances invaded the surrounding tissues. (2) If there is any doubt about localization, then the carcinoma may have already involved the chest wall, the pectoralis major muscle or the skin—it has become a doubtful or borderline case. (3) If the breast has become fixed and the carcinoma has invaded the pectoralis minor and major muscles or the skin to any extent, or the axillary lymph glands or the supraclavicular lymph glands, then the case is absolutely hopeless from the standpoint of surgery and should be subjected only to ray therapy. (4) Those cases should be grouped separately in which the patient is greatly emaciated, in which the tumor has undergone necrosis, and in which auto-intoxication has occurred. In Group 1 the localized cancers are placed and they should be treated with surgery. There is no excuse for anyone to treat a localized carcinoma of the breast with the X-rays or radium; it must be treated with surgery, because we know that radical excision of all cancer cells from a patient will cure that patient and nothing will do it as quickly or as well as the surgeon's knife or cautery. In a doubtful or borderline case the surgeon cannot be so certain whether all the cancer can be removed with the knife. In this case we should apply radium and X-ray and then follow with a surgical eradication. The clearly inoperable cases should be treated with radiations.

If we treat breast cancers along these lines we then combine the findings of the surgeon, the radiation therapist and the pathologist, and we will obtain results which can be compared and the methods of treatment may receive the proper evaluation. If we wish to determine which method of radiation is the correct one, the small, frequently repeated doses, or the one massive dose, we must follow up all our cases. If at the termination of three years it is shown that the small and frequently repeated doses give better results than the one large dose, we will all accept such findings. But unless we, as radiologists, follow up all our cases in order to determine the value of the treatment at the end of three or five years, we will never settle the differences of technic existing at present. Personally I shall always attempt to destroy the cancer by radiation in one sitting.

Dr. Francis C. Wood (New York): Many interesting things have been presented in this conference, especially in connection with the general theory brought out in the first paper, which have also been alluded to in the other papers, as, for instance, the question of the method by which the cancer cell is destroyed by the X-ray—is it killed directly by the rays, or is the destruction aided or wholly accomplished by an assumed natural resistance of the body? Certain experiments have been cited as pointing rather towards the fact that the body has a natural destructive power. Now without going into the thing too deeply, I would like to point out that the affirmative experiments are very few. They have mostly been done in one laboratory and with one mouse and one rat tumor. If these experiments are done with another mouse or rat tumor, the same results are not obtained. No scientific statement should be quoted as generally true without confirmation in other laboratories under different conditions and by different men, and I merely point out that a great deal of this hypothetical resistance which the body is supposed to have in destroying tumor cells is based upon entirely insufficient evidence.

Clinically we all see cancer growing through radiated tissue very freely and there is no evidence of any destructive power in such tissues nor of closure of the lymphatics, nor do animal experiments offer any evidence that raying closes the lymphatics. In other words, it is wise to be a little careful about the wide application of laboratory experiments using only one type of animal tumor. Every one should be willing to have a control on all experimental work and we should be careful about accepting this theory of the destructive effect of

the human body on a cancer cell on so slender a basis. Why does the body not destroy the cancer cell when it first starts? Why does the cell remain for five or ten years in an operative scar or a lymph node and then grow? The body has had a fine chance to destroy the cell during that ten years and yet has not done it. Those are a few of the clinical facts we have to consider in assuming that there are other factors except the direct destruction of tumor cells by the rays.

Dr. A. W. Crane (Kalamazoo, Michigan): I have been very much interested to hear from the surgeons regarding the localization of cancer. From reading Handley on Cancer of the Breast, I judge that this localization of cancer is almost never present. As soon as there is a palpable growth which is cancer, the lymphatics are already, according to Handley, invaded for a wide area about the growth and in every direction. There is also some question about a tumor which is not a cancer ever becoming translated into a cancer, excepting as cancer may start anywhere that there is sufficiently prolonged local irritation. If we consider those two facts, we can see that, in the first place, the surgeon would be vitiating his statistics as to the cure of cancer by counting in the cases of benign growths which he had removed—and thereby claims to have prevented the growth of cancer, if that be true; and also we can see that he would be under a misapprehension if he considered that he was able to remove all of the cancer cells. Now it is true that after the removal of a cancer which is not strictly local, the disease may apparently be cured, although cancer cells can still be demonstrated in the lymphatics around the area which was operated on.

I think that what has been said regarding statistics has not taken into consideration some of the actual X-ray statistics from foreign sources. A little over two years ago when I had the opportunity of hearing Holfelder at the clinic in Frankfort, he gave us X-ray statistics of the treatment of operable growths of the breasts which were both operated on and X-rayed. The results of the combined treatments were very much better than the surgeon alone could show. And in addition a certain number of inoperable growths may yet be treated successfully by X-rays alone.

I think we should meet the situation fairly, as to whether this question of teamwork between the surgeons and the X-ray men is worth while. I am convinced myself that, preceding operation, a growth should not be radiated. I have seen tragic results from a disturbance by the surgeon of a field that had been radiated. I believe—I state this dogmatically because perhaps it will bring out more thought and discussion—I believe that there should be a decision reached in the beginning: should this be an X-ray case or a surgical case? If it is to be an X-ray case then the surgeon should not touch it; if the surgeon does operate, I believe that he spoils it to a large extent for future radiation nothwithstanding Holfelder. In a great many cases the seeding-down of the patient is accomplished at the time when the surgeons open up the lymph spaces and disturb the tissues in ways which are difficult to account for as yet. Certain it is that when the disease is widespread, the radiologist is often accused of scattering the disease, when, in reality, the patient has been seeded by events at the time of the operation.

I believe that we should have reliable statistics. They would have to be obtained from cases which had been radiated only and from cases which had been treated only by surgical means. We have heard that statistics may tell any kind of a story. That is certainly true where they are not complete. At the Boston meeting of the American Roentgen Ray Society we had a distinguished visitor, Dr. Forssell of Stockholm, Sweden. He gave us an example of statistics which were really beyond criticism, because, for a period exceeding five years, every case that had been treated in his radium and X-ray institute (which is under government supervision) came back at intervals for examination at government ex-

pense. Every case was recorded and thus these statistics took account, not of some cases, but of every one. These statistics of the radiation treatment of cancer of the uterus and cervix (radiation by X-rays and by radium), given by Forssell, it seems to me settle for all time the fact that this disease is not now a surgical problem but is exclusively a radiation problem. I do not think that we should allow the surgeons to make the assertion that at any stage in the growth of cancer operation is the best treatment. Perhaps it is, but we should at least take the position that it is an open question, and I believe myself that the time will come when the surgeon will no longer touch a malignancy anywhere in the body.

Dr. W. L. Ross (Omaha, Nebraska): I wish to speak in reference to the third effect the first speaker brought out, of the X-ray upon the tissues, and that was the biochemical effect that is produced in radiating a tumor of any kind or any tissue of the body. I am heartily in accord with the biochemical effect which is produced by raying short of a ray or a dose strong enough to produce autolytic solution of the tissues of the tumor and surrounding cells; otherwise the fractional dose of the X-rays used on a tumor of any kind. Now, he proved by his slides that the ray did destroy cancer cells. He also exhibited some slides in which the cancer cells were still active. I wish to bring out the fact that if we can increase the biochemical effect of the cell element adjoining the cancer tumor, thereby we have hastened not only the elimination of the cancer cells but prevented the further spread of the cancer cell. This can be brought about by physiotherapy, and you will notice that all the way through this symposium there has been emphasized the fact that there is a lowering of the vitality, of the resistance, of the whole system in a patient suffering from cancer; otherwise the patient is sick. The fourth speaker said that surgery and X-ray offered all there was to be offered, or the most, anyhow, to be offered in the cure of cancer at the present time. I wish to emphasize the fact that we are omitting the best—one of the best—factors when we do not use physiotherapy in building up our patients; not only the local but the general resistance, and the sedative form of diathermy can increase the blood supply locally, and with it, properly used, stimulate and build up the great sympathetic nervous system. I wish also to emphasize the fact that any tumor of the breast is to be treated, or should be treated, by X-ray, and since the surgeons bring out the fact that the greatest percentage of cure or relief is in the beginning so it is with the X-ray. The earlier you can treat the case of a tumor of the breast, no matter whether it is malignant or benign, the more certain you are to relieve that patient of that tumor. If the patient is relieved of a tumor, that, to her, is what she applies for and nothing else.

Dr. A. U. Desjardins (Rochester, Minnesota): Dr. Wahl in his paper mentioned a few things which may be taken as examples of a difference in the point of view, such, for instance, as his allusion to roentgen toxemia. This has no particular reference to cancer of the breast, but I mention it because many physicians, surgeons, and even radiologists, who have read about the experiments of Whipple and his co-workers, Martin and his associates, have misinterpreted the findings there given. The effects produced under the conditions obtaining in those experiments are undoubted and unquestioned, but the fact that the intestinal mucosa is very susceptible to X-rays in certain dosages does not at all explain the general problem of roentgen toxemia. One can expose a tumor of the brain to radium or X-rays; such treatment may be given to tuberculous glands of the neck, or, again, to certain lesions of the extremities, and roentgen toxemia will frequently be observed. Under those conditions certainly the intestine has nothing to do with the toxemia.

Concerning the co-operation between pathologist and radiologist it may be said that many pathologists, in fact, the major-

ity of them, know nothing about the effect of radiation on tissues and most of them are not interested in it. This is unfortunate, and I hope it will in time be corrected, because only by such collaboration can many of our problems be solved.

I wish to congratulate Dr. Jackson[1] on his remarkable statistics. They are very creditable indeed and show that he has been able to impress his patients with the necessity of coming to him early. Dr. Jackson asks for figures and statistics and this request is a perfectly natural one; we want such statistics ourselves. However, if such statistics are ever to be obtained, surgeons must either turn over cases to the radiologist or else co-operate with him in dealing with certain types of lesions. No radiologist can ever satisfy Dr. Jackson unless he is given an opportunity to work on a sufficient number of cases to produce statistics. At the Mayo Clinic we have been making an attempt to obtain such information but it will take some time, because we have to allow a three- to five-year period to elapse. The 1922 series was treated before and after operation; since 1922 only post-operative treatment has been given. After an interval of five years these cases will be reviewed in separate groups and we will then adopt whatever method proves to have been the best.

One of the main points of difference of opinion among surgeons on this subject is the question of operability. With an eye to good "statistics" some surgeons are extremely careful in selecting their patients for operation, while others with less knowledge and experience tackle everything. If the axillary glands are extensively involved, operability is at least doubtful. There are cases where for special reasons it may be advisable to undertake a so-called palliative operation; but when metastasis has gone above the clavicle it is at least likely to have gone still farther. Most surgeons wisely refuse operation under such conditions.

[1]Dr. J. N. Jackson's paper has not been received for publication.—Editor.

Dr. W. S. Lawrence (Memphis, Tennessee): I want to begin about where Dr. Crane left off. I have always been impressed with the fact that cancer of the cervix is very, very amenable to X-ray and radium treatment. From my own experience, if I had to judge from that alone, I would always welcome one of these patients to the office, because I feel that I can do a great deal for her, whatever may be the stage of the disease, but particularly if it is in the so-called operable stage. My personal opinion is that of Dr. Crane exactly, that carcinoma of the cervix is no longer an operable disease. I am far from standing on the same ground in carcinoma of the breast. I have often wondered why carcinoma of the breast does not seem to be as amenable to X-ray treatment as carcinoma of the cervix. It would seem that carcinoma of the cervix is located in a much more dangerous region to be radiated. Treatment through Martin's susceptible gut region would appear to be much more apt to give roentgen sickness, and still we get results there and the patients stand the treatment well. Carcinoma of the breast being in the upper region of the body, it would seem that it would not give us the roentgen sickness to an extent to prevent giving that amount of treatment which the tumor, in reason, should require; and still, from my own personal experience, I have never been able to do the same work on carcinoma of the breast as I have on carcinoma of the cervix. Personally I have never cured a primary carcinoma of the breast. I would like to hear from some of those men who have. It may be partly because I have never pushed the treatment to the safety limit. I have always held the X-ray on one side of the question and the surgeon on the other, and possibly have relied too much on the good work which I know the surgeon can do in cases of this class. I think it would be valuable if each man here could give us something of his own experience. Person-

ally I have never benefited a case that had fluid in the chest; I have never seen a carcinoma of the breast case improve or derive the slightest benefit from radiotherapy after it had gone to the stage of getting fluid in the chest. I have never seen a primary case that was inoperable that did not improve if it had not reached that stage. They all improve up to a certain degree, but I have never been able to cure one. I stand with the surgeons, so far, but I would like to stand where Dr. Crane stands with the radiologists.

Dr. Axel Reyn (Copenhagen, Denmark): I beg you to excuse my poor English,—that is the first thing I would do. On this question of treating cancer of the breast with X-ray or radium, I would like to say that our opinion in Denmark is that you should never treat a case which can be operated on. Concerning the cases which are inoperable, I can tell you that we have never seen a real cure. It is true that many cases get better due to the X-ray treatment, but they are not cured, and the reason why is that we do not destroy the cells in the depth of the tissue. I have treated many cases of skin cancer with X-rays and have found peculiar things in these cases. I have extirpated twelve cases, after they were treated with X-rays. They were perfectly cured—I could not find any point clinically where they seemed to be affected; still, on making sections of them in series, I have found small nests of cancer cells in the tissues. If you cannot cure cancer in the skin you cannot cure cancer in the chest. We never treat an operable case with radium or X-ray and I warn you against such treatment, because the patients will be disappointed—I have seen many, many cases of that sort.

Dr. H. R. Wahl (closing): Relative to the question of radium toxemia, I did not want to give the impression that the toxemia was due to a lesion of the intestinal tract. I simply mentioned this as one of the explanations that has been advanced to explain the toxemia. I also gave several other explanations. I do not know what the real cause is. Some say that the toxemia is due to injury to the adrenal gland. Warthin says it is due to action upon the liver. Those who are especially interested in this subject ought to read Davis' work on the effect of prolonged X-ray exposure of the chest. He has found marked thickening of the pleura and localized fibroses of the lungs. I wish to emphasize that we do not know exactly what the X-ray does and why it does certain things.

In the discussion of this symposium one of the speakers questioned the part that the defensive mechanism of the body plays in explaining the radium reaction, because the body does not attack the cells at first. Injurious agents frequently enter the body and often it is only some time after their entrance that the body seems to develop a resistance against them. For instance, the colon bacillus may develop in the body, which may become accustomed to its presence and then, following the injection of a colon vaccine, the formation of more defensive substances are stimulated, with destruction of these organisms. Because the body did not kill these colon bacilli at the very beginning does not mean that the body has no power of producing resistant forces against them. The same may also be true of the arrest of the development or resistance against cancer cells by the body after they have once begun to develop, and the subsequent stimulation of these resistant forces by exposure to the X-ray.

One of the main propositions that I wished to bring out in this paper was the value of pathological examinations of lesions treated, in ascertaining just how the X-ray and radium work. I feel that the surgeon has a little the best of the argument over the radiologist for the simple reason that the surgeon usually has a control of his work, in that he has some tissue which some one has examined. The report and the slides can always be referred to, to show that his diagnosis of the condition is either correct or wrong. The radiologist often

applies the treatment without certain knowledge of the lesion with which he believes himself to be dealing. He has no concrete evidence after the condition is cured to demonstrate to some other person what he had to begin with, such as the microscopic slide of the lesion that the surgeon usually has. He lacks the concrete evidence to show that he has dealt with a carcinoma. On the other hand, if the radiologist would remove a small piece of the tissue just before treatment he would always have a control for his treatment, showing exactly what he had to begin with. The results of X-ray and radium will depend largely on whether the dose has been graded correctly, for if the dosage is too large or too small the results are not going to be good and may even be disastrous. A correct dosage depends a great deal on the nature of the growth and its location. How are you going to tell its nature, just by looking at it? Even a competent pathologist sometimes is at a loss as to the exact nature of a growth by glancing over the gross specimen. A small bit should be taken out, some competent man should pass on it and tell what its nature is. If this is done it will be found that the reaction of tumor to X-ray varies a great deal with the nature of the growth and its histological structure. Even different parts of the tumor may vary in their response to a given dose. In most cases no harm will come from removing a small piece shortly before the treatment is given. A number of radiologists do this and do not find serious results from the biopsy examination.

DR. J. F. MCCULLOUGH (closing): I do not know that I have much more to say. There is one condition, however, namely, the advisability of using X-ray in terminal cases. It is pretty hard to determine exactly when a patient's reserve is all gone. Sometimes even in the most hopeless cases they will come back pretty strong. I have had a case of metastatic carcinoma involving the upper third of the femur, in which there was destruction of all but the cortex of the greater trochanter. This patient was put to bed and subjected to intensive X-ray treatment, with the result that the femur recalcified and the patient was able to carry on for two years. She was free from pain and able to go about her daily duties without difficulty. She finally died from metastatic liver involvement.

So far as pre-operative radiation is concerned, if this is to be demonstrated as good procedure, it will only be after the surgeons have recognized its value and tried it out.

Irradiation of tonsils.—The tonsil is an important organ and should be conserved through the adolescent period when possible. Irradiation has a known and well established effect on the essential tonsillar tissue. Irradiation can be applied effectively, accurately and with safety to the tonsil. When the pathologic changes are of the hyperplastic type, in which atrophy of the tonsil and re-establishment of drainage is the consummation to be desired, irradiation is indicated. When irremediable damage has been done to the tonsil, or when atrophy and re-establishment of drainage is apparently not to be expected, irradiation is not the treatment indicated, but surgery, if clinical conditions call for radical treatment.

W. W. WASSON, M.D.

Pathologic Basis for Roentgen-ray Treatment of Tonsil Disease. W. Warner Watkins. Jour. A. M. A., Oct. 25, 1924, p. 1305.

IS CANCER A TRUE DISEASE OR MERELY THE RESULT OF A CONDITION OF CHANGE IN THE GENERAL ORGANIZATION OF THE ORGANISM?[1]

By MONTROSE T. BURROWS, M.D., St. Louis, Missouri

From the Barnard Free Skin and Cancer Hospital, and the Department of Surgery, Washington University School of Medicine, Saint Louis, Missouri

THE problem that confronts the X-ray and radium therapist is not one of cancer prophylaxis, but the cure of the disease fully established. Many of the older writers had already concluded that cancer is not a disease in the sense that typhoid fever is a disease. It is not the result of a specific foreign parasite, but merely the result of some change, either in the cell or its environment. This idea is well exemplified in the work of Thiersch, Remak, Boll, Cohnheim, Ribbert, and others. Other authors in recent and older times have taken the other view. This other view has been recently revived by Edwin Smith, Ochsner and Nuzum. Smith based his conclusion on the identity of a cancer-producing organism in the crown gall of plants, the *B. tumefaciens.* Ochsner draws his conclusion from the fact that Nuzum has demonstrated bacteria in certain human cancers and has apparently excited the development of the disease by inoculating them into animals.

Against this parasitic view of cancer comes the interesting and recent work with coal tar, X-ray, radium, etc. While this work has shown that cancer may be induced by any one of a number of conditions and substances, such as bacteria, coal tar, other lipoid solvents, X-ray, radium, chronic inflammation, congenital tumors and defects, etc., it has not shown that the cancers, once induced, are in any way concerned with any of these conditions or substances. It is too late for the Irishman to discard his pipe after his cancer has developed. Coal tar is essential in developing coal tar cancers, but the cancers, once induced, then proceed independently of the tar. Many cancers thus induced have been transplanted through many generations of animals. These cancers have grown undisturbed long after the coal tar had entirely disappeared.

The impelling forces of cancer, as seen in the light of these facts, are in the cell or the environment about the cell. The growth in cancer is not due to external agents, but to the relieving of the cell from the influences of the body so that it may grow and divide independently. Cancer will become known, therefore, when those general conditions, which regulate growth and function in body cells, become known.

It thus became of interest to study the general conditions regulating the growth of body cells as they are seen in the tissue culture and to deduce, if possible, the relation of these conditions to the general conditions peculiar for the growth of cells in the body. The theories deduced by the older writers, one may readily group into two classes: one of these, of which the Cohnheim theory is paramount, assumed the change to be primarily in the cell; the other view, of which Ribbert is one of the chief supporters, considered the change to be in the environment about the cell.

As Ribbert clearly points out, there is no evidence that the cells of the mature organism have lost their power to grow. The fact that they grow readily after injury rules out this possibility. Growth and function are sometimes determined largely by the environment about the cell. While Ribbert and the school which followed him failed to find the nature of the environment suitable for an active independent growth of cells and the impelling forces for growth in the wound, the exponents of the change being primarily in the cell lost ground continuously, as the various morphological peculiarities of the cancer cells were shown to be readily reproduced by producing the

[1]Read before the Radiological Society of North America, at Kansas City, December, 1924.

proper environment about normal cells. Among these peculiarities are the cell inclusions, the staining properties of the cells, the shape of the cells, their arrangement and peculiarities of division, and the formation of their chromosomes. Again the earlier writers, such as Driesch, Hofmeister, Sachs and DeBary, had already noted a definite relation between growth and the structure of the whole organism and not one related to the cell. Driesch's work has also shown that the growth of the cell in the normal organism may be influenced by mechanical as well as chemical conditions in its environment. He found that when the gastrula of the sea urchin is cut into two, the two halves do not grow at once, but only after each half has reformed into a perfect gastrula of one-half the size. This remolding is the result of a movement of the cells. Growth does not take place until this remolding is complete.

Bardeen and Morgan have shown that the growth of regenerating tissue does not depend on food and oxygen alone. Morgan finds the legs of salamanders regenerate as rapidly in starved as in well-fed animals. The difference between the two is that the starved animals suffer extreme emaciation from this growth, as well as from the lack of food.

The nature of these more subtle factors or stimuli regulating and controlling growth has not been found. In my early studies with the tissue culture, I undertook this problem. In these studies (1) (2) I noted that body cells will not grow under all conditions in a culture, when blood plasma is used as a medium. For these cells to grow it is necessary that they be crowded together in a stagnant area of medium. Single cells will not grow. Growth intervenes only about densely cellular and compact fragments placed in a small amount of medium. Growth may be inhibited by teasing these fragments apart and by placing them in a large amount of medium, which can more easily absorb and remove products formed by them.

Under these conditions of stagnation and crowding, it was further noticed that growth does not commence at once, but always after a latent period. This latent period is much shorter about fragments of an actively growing tissue, such as tissues of embryos, cancer and growing granulation tissue, than about normal non-growing adult tissue. As the growth rate of any organ progressively decreases from early to late life, so fragments of this organ placed in a culture show a progressively longer and longer latent period, before any activity is seen in their cells. The cells from a millimeter thick fragment of a five-day-old chick-embryo will begin to migrate as early as one to two hours after the cultures are prepared. Growth is well established in these cells twelve to twenty-four hours later. No migration of cells is seen from similar fragments of a ten-day-old chick-embryo fragment before six to eleven hours, and growth rarely intervenes before twenty-four to forty-eight hours. About fragments of a fifteen-day-old chick-embryo heart, migration begins after twelve to twenty-four hours (3). Growth may intervene after forty-eight to ninety-six hours, but it may fail entirely unless these older fragments are transplanted to new drops of plasma every twenty-four hours for three to several times.

This necessity of stagnation and cell-crowding for growth indicates that this process must depend on the accumulation of some products in the tissue fragments. The latent period shows again that this must be true and that this product or products must be formed by the cells.

To prove the existence of such a substance, I extracted, immediately after they were removed from the body, many fragments of normal non-growing adult tissue, the slower growing tissues of older embryos and the actively growing tissues of young embryos and cancer. Small fragments of these same tissues were also placed in stagnant hanging drops of plasma, where they were amply supplied with oxygen, but otherwise freed from any effect of the cir-

culating blood of the body. After several hours or days these fragments were removed and extracted in the same manner as the fresh tissues had been extracted. The extracts of all of these tissues were made by grinding in a mortar, equal weights of tissue with an equal weight of isotonic salt solution. The clear supernatant fluid was then added in equal parts to plasma and used for medium. Carefully washed isolated embryonic cells were used for testing. These isolated cells will not grow in pure plasma or plasma diluted with isotonic salt solution. In the presence of the extracts of growing tissues from the body, such as the tissues of young embryos, cancer and granulation tissue, these isolated cells showed migration and, in many instances, active growth. No such effects were obtained from the extracts of the tissue of older embryos and adults, when the extraction was made as soon as the tissue was removed from the body. On the other hand, if these same fragments of adult tissue are left in a stagnant drop of plasma, which is supplied with oxygen, they develop this substance in the course of one to six days, depending on their age.

In a further analysis, I attempted to see, then, how this substance is formed by the cells in the stagnant cultures, whether the actual quantity of it present in the tissues varies the reaction of the cells and is important in determining the growth reaction and (3) whether it might be washed away from actively growing cells by the circulating blood in the body. It has been seen that many fragments do not contain the stimulus when removed from the body. They develop it after they are taken away from their normal circulation and placed in the stagnant culture in contact with the same blood plasma which had previously bathed them in the organism.

In studying the formation of this substance in fragments of tissue in the culture, it was noted that it failed to accumulate, except in the fragments well supplied with oxygen, and the amount formed is directly proportional to the number of cells per unit area in the fragment, and the amount of oxygen consumed. In the fragments of older tissues, which contained no noticeable amount when extracted in the fresh, it took more oxygen to accumulate a measurable amount of this stimulus than in the younger fragments which already contained a limited amount (4).

From these observations, it became evident that this stimulus is a product of the cell's oxydations. In further experiments, I attempted to see if oxygen is necessary for the other reaction of the growth of these cells. In these experiments it was found that growth will proceed in the absence of oxygen as long as the stimulus is present (4). Oxygen, as it became evident, acts only in producing the stimulus. This led me, therefore, to look at this stimulating substance as something comparable to the heat of the steam engine and to name it the *archusia* or driving substance of the cell. It was evidently the accelerator of all reaction of the cell (5).

Further quantitative studies of extracts of young embryonic tissue and cancers, which contained large quantities of the *archusia* (S) showed that low dilutions (S^1) of it have no effect on isolated cells. In slightly greater concentrations (S_2) it acts to stimulate the cells to migrate into fixed proteins and fats and to take up mobile particles of protein and fat from the medium, and store them. In still higher concentrations (S_3) the cell digests the protein and fats and grows and divides. In all higher concentrations (S_4) the cells themselves are digested (6).

In many cultures, I forced a stream of serum, 1 part, and isotonic NaCl solution, 1 part, over and through the medium about actively growing cells. The diluted serum was passed along the fibers of a cotton wick, laid in the medium. When the serum is passing, growth is inhibited. When it is stopped, growth intervenes (7).

The effects of such an accumulation of products of the cell and its necessity for growth are easily shown in cultures where two fragments of any tissue are placed close

together. In the interval between two such fragments, substances coming from both fragments accumulate in greater concentration between the fragments than about other parts of the periphery of either fragment. Figure 1 is a photograph of two ¾ mm.

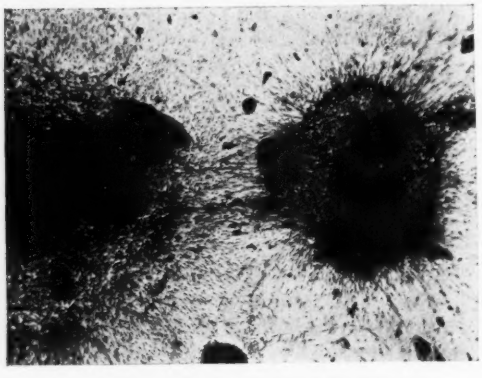

Fig. 1. A photograph of a simple hanging drop culture of two fragments of the eyeball of an eleven-day-old chick-embryo, showing greater growth at the interval between the fragments than elsewhere.

thick fragments of the eyeball of a chick-embryo placed ¾ mm. from each other. Note the active and greater growth of cells in the interval between the fragments.

It became evident in the light of these facts that a growth of cells in the body may be due to two factors; the passage to them of the growth-stimulating substance from other sources, or to a crowding of the cells together and a reduction in the blood supply to the mass. By the latter mechanical changes they were able to either induce the formation or accumulate this growth-stimulating substance in and about themselves.

It thus became of interest to see if all actively growing tissues of the body had this particular organization. It is a well known fact that the nails, hair and bone marrow have an independent growth in the organism. The most active normal growth is in the earliest periods of embryonic life. This active independent growth wanes as the blood vessels develop and the cells become separated. During the very active growth of the liver its circulation is through large sinusoids and is sluggish. I have found that the circulation at the outer end of the nail bed is reduced to a single layer of large sinusoids, which are filled by vessels of much smaller caliber. The bone marrow circulation is also sinusoidal and sluggish. Cancerous tissue is characterized by being densely cellular. Boll, many years ago, noted the peculiar, irregular, distorted and partly occluded blood vessels in many cancers. The capillaries are few in proportion to the cells in all cancers. In other cancers the blood vessels are large and the circulation is sluggish. In all cancers blood vessels are being destroyed at all times in the more crowded regions. In the wound, as I noted in a recent paper, the growth of cells is not related to the defect, but to the areas which are suffering from a reduction in their circulation either through a previous destruction of their blood vessels or an inflammatory slowing of their circulation (8).

In the studies on wound healing (8), I also noted that any dense stagnant mass of cells in a tissue not only grow, but they prey on neighboring tissues and blood vessels. They reduce these less crowded neighboring tissues to a hyaline mass. Such a dense mass of cells, as is found in cancer, may thus continue to reproduce itself and grow indefinitely. It destroys the normal blood supply and tissues ahead of it and grows continuously to form a dense mass of cells which degenerates in its central portions.

In the experiments with human and animal cancers there has been no evidence to show that the cancer cells are different in their requirements for growth than the normal cells. Single cancer cells cannot grow in plasma. The growth of these cells demands the same crowding as the growth of normal cells. The cancerous tissues differ from the normal cells in that the fresh extractives are somewhat more toxic than those of equally active growing embryonic tissues. In the cultures normal cells degenerate after an active period of growth. This degeneration comes on more quick-

ly in cultures of cancer. This is in proportion to the original greater crowding of the cells in the cancer. Whether it may be related also to other factors in the environment of the adult where cancer

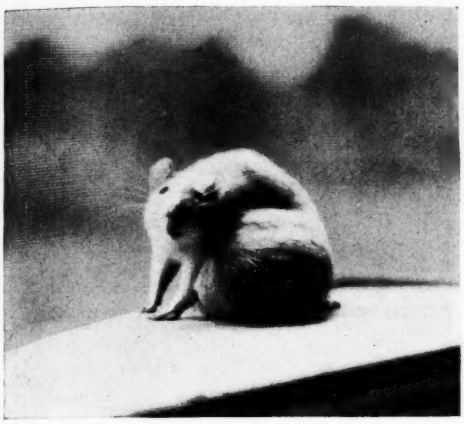

Fig. 2. A photograph of a rat having a sarcoma produced by altering the arrangement of cells in a fragment of normal embryonic tissue transplanted beneath its skin.

exists, I do not know. It is possible that both these factors play a rôle.

From these observations it became evident therefore that cancer may be nothing more than the result of any condition or substance which may primarily reduce the circulation to a cellular tissue or build a local dense mass of cells, which has a lowered circulation. To prove this idea, it became of interest to see if cancer may be produced by such procedures. In the tissue culture the cells of cellular tissue fragment disperse into the medium. Previously formed structures may be thus rent asunder. Blood vessels are destroyed by their endothelial cells moving apart. The *archusia* extracted from actively growing tissues also stimulates the cells to grow in these fragments. These cells do not grow to form normal structure—they grow to form dense masses. Structures such as the blood vessels, epithelial tubes, etc., are lost in this proliferation. Fragments of fifteen- and sixteen-day embryos were treated, therefore, for twenty minutes with a Berkefeldt filtrate of an actively growing sarcoma and injected with the filtrate under the skin of adult rats. In 91 per cent of the animals the tissues of the fifteen-day-old rat embryos failed to grow to any extent. The

Fig. 3. A photograph of a section of a carcinomatous ulcer developing after four months of continuous low pressure on an area of skin of an adult rat, which had been injected at the beginning of the experiment with 1 c.c. of a Berkefeldt filtrate of a Jensen rat sarcoma.

blood vessels had been completely destroyed in these fragments. In 9 per cent, the growth was greatly stimulated and a sarcoma developed in one of these. This was a very malignant tumor. It was transplanted through nine generations of rats and proved fatal in over 95 per cent of the cases. These fragments had suffered only a decrease in their blood vessels. Sixteen per cent of the tissues of the sixteen-day-old rat embryos were stimulated and one sarcoma of the same kind as the former developed (Fig. 2). In the other rats the tissues of the sixteen-day-old embryos failed to grow in the presence of this high concentration of *archusia*. In other experiments, I tried the effect of a continuous reduction in blood supply to the normal skin by applying a continuous pressure. Atrophy and simple ulceration alone resulted. Fifty simple ulcers thus produced remained as long as six months to a year and a half, without showing any malignancy. In a third group of animals, I injected extracts of thirteen-day rat embryos or a Berkefeldt filtrate of a Jensen sarcoma into the skin

before applying the pressure. In these cases the cells of the epidermis and gland suffered hyperplasia. The atrophy and ulceration, which followed the action of the pressure in the previous cases, were either greatly delayed or carcinomata developed (9) (Fig. 3).

Having thus established by direct experiments that cancer may be the result of these simple changes in organization, it became of interest to see how coal tar, other lipoid solvents, bacteria and other agents produce this disease.

THE ACTION OF COAL TAR AND OTHER LIPOID SOLVENTS

In a study of cellular migration, it was of interest to notice that body cells are not possessed of any complex means of propelling themselves, such as the walking of man, the ciliary movements of many bacteria and the paramecia. They move by liberating a surface-tension-lowering substance. This substance is peculiar in that it fails to decrease the surface tension of water, but is specifically absorbed only by the primary food constituents of the cell, proteins and fats and substances having like affinities (5). A cell liberating this substance into a medium draws the mobile proteins and fats to it. It is drawn into fixed masses of proteins and toward larger masses of fat, which have a greater inertia than the cell. It became evident, therefore, that coal tar may act to build a dense mass of cells capable of cancerous growth through its ability to draw cells to it away from their blood vessels and intercellular substances. Such a dense mass of cells must sooner or later acquire the property of growth and increase in mass.

Jorstad (10), working in the laboratory, has studied the effect of coal tar in the tissue. He finds it acts alone in this capacity. Drops of coal tar collect the cells from the surrounding tissue. They absorb and become saturated with the surface-tension-lowering substance of these cells. They do not stimulate the cells to grow. Growth intervenes when the mass of cells about the drop of tar reaches a certain density. Such a mass of cells can be accumulated by the tar only when it is placed in a cellular tissue. In a less cellular tissue, as the normal subcutaneous connective tissue of adult rats, too few cells are collected often for growth to intervene. These few cells not only fail to show growth, but shrivel as their lipoid soluble substances are lost to the tar.

THE ACTION OF BACTERIA AND THE NORMAL STIMULUS FOR LIFE IN THE BODY

According to the formulation presented by the above observations, growth is dependent on the presence of a certain concentration of a growth stimulus about the cells. This growth stimulus is formed by the cells normally when they are crowded together in a stagnant environment and supplied with oxygen. I have shown that this is true for the cells in the body as well as in the cultures. In the cultures it has been noticed that this stagnation must be excessive for growth to intervene. It must be more excessive than the stagnation which exists about the cells in most parts of the young child. This suggests that special means are necessary for supplying this substance to the cells of the child in order that it may grow. From the study of the nutrition of children, it has been shown that certain substances, aside from proteins, fats and carbohydrates, are essential for growth. These other essential substances are the vitamines. Two important vitamines are designated as A and B. A is fat-soluble, B is water-soluble. It has been shown above that the cells migrate by liberating a fat-soluble substance. Coal tar absorbs this substance in drawing the cells to it. The cells suffer by the loss of this substance to any more than very small quantities of tar injected subcutaneously. Larger quantities of tar lead always to the emaciation and death of the animals. Noting the relation between the growth stimulus, the *archusia* and vitamine B and this fat-soluble substance of the cell and vitamine A, it became

of interest to see what relation they may have to each other.

Jorstad investigated then the toxicity of coal tar and the relation of vitamine A in counteracting it. He finds the toxicity of the tar is readily counteracted by feeding butter-fat and cod liver oil. These substances contain vitamine A.

Bacteria, as it is known from the work of Edwin Smith (11), must induce the cancerous formation in plants not through drawing the cell to them, but through inducing an active local growth of a few cells. They produce thus the same cancerous organization, not by collecting cells as the drops of coal tar produce it, but by stimulating the growth of a few cells. We have investigated these organisms in relation to vitamine B and find them to be readily substituted in the diet of animals for vitamine B, but not for vitamine A. When fed they allow and stimulate the growth of the animal. When injected locally they stimulate the growth of the cells about them and produce a cancerous organization.

Function, we have found in the study of heart muscle cells, is the result of polarizing the cells. This polarization is brought about by the growth of blood vessels between them. This growth of vessels hinders and prevents growth. Function is something which has developed at the expense of the growth mechanism in the cell. The body is able to grow only as it is able to acquire a part, at least, of its growth-stimulating substances from other growing plants and animals. Our high functional state, as is evident, therefore, has been made possible only through an evolutionary development. Higher forms of animal life exist as such only as they can acquire, in part, at least, the life energy from lower growing and non-functioning forms.

We have also sought a source for this stimulus in other parts of the body. It is well known that the glands of internal secretion play a definite rôle in promoting growth. The hypophysis acts in this capacity on the skeleton. The sex glands liberate substances which act on the general metabolism of the organism. It thus became of interest to study directly the effect of the secretion of these organs on the growth of cells in general. Recently, Allen and Doisy (12) isolated the active hormone of the ovaries. Johnston and the writer (13) have been studying the action of this hormone by a newly devised method. Inert fats, such as mazola or corn oil, have been injected into the subcutaneous tissue of rats. Droplets of these fats remain in the tissues for a long time, becoming encapsulated by a collar of fibroblasts, much as coal tar becomes encapsulated. In other experiments, ovarian hormone was added to the fat. The connective tissue cells invaded the oil, which contained the hormone, grew most actively and consumed it. These cells digested this fat, as the cells of the culture digest the fat, either after they have accumulated the *archusia* about them, or it has been added to the medium. These latter facts have a significance not only in showing directly why the woman accumulates fat at her menopause, but for explaining the development of cancer at this period. It is a well known fact that if one bud of a limb be stimulated, the others atrophy. Cancer, as I have described it, is a normal growth of cells, which becomes abnormal only because of its location, its eventual destruction of its own circulation and the associated necrosis and its abnormal fermentative processes. In an actively stimulated organism such growth must proceed with difficulty. For the cancer to grow it must produce a great amount of energy in order to overcome the normal resistance of the tissues about it. It is therefore apparently not unusual that cancer should be a disease of the aged. It must be much more easily produced at the period of decline or when growth energy is much lessened in the body as a whole.

CONCLUSION

No attempt has been made as yet to investigate the action of X-ray and radium. It has long been known that these rays may not only cure cancer, but induce its forma-

tion. It has been shown above that the same stagnation and cell-crowding which leads to growth will in a greater degree lead to the destruction of the cells. Wolbach (14), several years ago, showed that the rays of X-ray act on the blood vessels to destroy them as such. Recently Steenbock and Black (15) have shown that the rays from a quartz mercury lamp will liberate growth-promoting substances in liver and muscle of rats.

As I have just stated, we have not studied as yet the action of the rays of radium and X-ray. The object of this report has been to bring facts before you which may add materially in making such analysis and which I feel show quite definitely that cancer is not a disease in the sense of the infectious diseases, but that it is the normal reaction of body cells in a particular environment. It is to be classed, therefore, with gangrene and atrophy. Gangrene became understood when the necessity of oxygen became understood. Gangrene results from any condition which stops the flow of blood to a part. Cancer comes into existence when the normal arrangement of cells and blood vessels is disturbed, so that the cells become sufficiently crowded in an area of reduced circulation. These conditions lead, in the presence of oxygen, to the formation or the accumulation of an active growth-stimulating substance. The eventual cure and prevention of this condition will be made, therefore, through the use of quantitative changes in the whole—and not qualitative ones. These necessary changes will become known through the more exact knowledge of those substances and conditions, known to be able to produce and also destroy cancer, such as X-ray, radium, etc.

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DISCUSSION

Dr. Edwin C. Ernst (St. Louis): This interesting newer phase and line of attack upon the cancer problem certainly merits a most critical and careful consideration. I wish to state at this time that I am grateful to Dr. Burrows for having had the opportunity of working with him at the Barnard Free Skin and Cancer Hospital, and being thus, by co-operation, likewise allowed the privilege of helping to analyze or establish facts as to the effects of X-ray and radium radiations upon body structures, and their relation to cell reactions, beginning with the very first normal tissue changes and extending to the period when definite cancer has been established.

The problems confronting us are many, although some of these investigations are comparatively simple because the bio-chemical, normal and pathological foundations or groundwork have been so carefully and interestingly developed and described here by Dr. Burrows. Nevertheless, we realize the difficulties confronting us in attempting to further develop and more thoroughly understand the theoretical considerations as

they have been presented, especially the possible relationship of the various types of radiant energy to normal and pathological cell changes, both from the scientific laboratory and the clinical standpoints. The probable actual close relationship of the human and animal cell phenomena is the second great problem which confronts us and has been the most difficult stumbling block and barrier between animal experimentation in cancer research and the human clinical phenomena. This wall or barrier is frequently longer and higher than the old Chinese wall, in fact so much so that successful animal experimentations are at times completely isolated and thus are found to be of no practical value. Human and animal tissue actions or reactions to cell stimulation are frequently at variance and do not check. The definite actions or reactions of the cells in the one cannot be duplicated in the other.

The experimental phenomena described and discussed here certainly appear to be fundamental. Cell growth actions and reactions follow normal and pathological irritations and stimulations with a uniformity that certainly suggests the probability of an unusually close relationship between the two, although there will always be certain fundamental differences.

Normal phenomena of human and animal experimentations throughout the early stages are merely a matter of normal and abnormal cell arrangements or disarrangement.

The findings certainly warrant the assumption that there is a direct and indirect effect upon the intra- and extracellular fluid constituents of the tissues under the influence of specific quantities of absorbed X-ray or radium energy. Our great problem, therefore, may prove to be simply one of applying a quantity of radiant energy sufficient to control these complex substances. Such changes apparently did bear a direct relationship to the cell and its surrounding structures whenever the fluid concentrations were either increased or decreased, and thus were found to be either beneficial or harmful to either the normal or abnormal pathological cell groups.

Therefore, we made every effort to standardize the introduction of radiant energy of X-ray into the deeper tissues of the body and adopted technical methods applicable to the higher, medium or the lower voltages of our machines for both the human and the animal experimentation, which methods of measurement are, we believe, and in fact have found them to be, a practical means of duplication of the respective higher or lower voltages of X-ray energy within minimum limits of error in dosage, thus controlling the radiant energy absorption.

There is nothing new or original about the method which I hope I may find sufficient time to describe before this body. The mechanical and physical features have been simplified rather than complicated, nevertheless they are similar to the usual methods of measurement adopted by the trained physicists. I present them to you as installed at the Barnard Free Skin and Cancer Hospital, and thus far they have proven to be very practical—almost foolproof—yet admirably efficient in every way.

As stated above, the energy can be accurately duplicated from day to day and from month to month.

We all realize after what has been stated at this meeting that in order to intelligently report our results, the amount and quality of X-ray administered must in every case be capable of duplication, and they must be intelligently understood by each and every radiologist. Most important of all is it that the dosage should be both accurate and possible to duplicate. We all realize that variations in doses must of necessity produce different physiological and biological effects.

Conditions beyond our control do change the radiation output of our transformers, perhaps without our knowledge or that of our assistants. Any method of operation is valueless unless repeated checks or controls can be employed, so that the X-ray energy output will not only be uniform from hour to hour, but also from year to year.

Personally, I have found and continue to find it necessary to repeatedly eliminate mechanical and physical sources of error in our installation, since the ordinary sphere gap measurements, milliampere readings, etc., are indeed very limited by themselves in their respective valuations in relation to the changes in the output of our machine, in the hands of the ordinary radiologist or assistants employed. However, we should always take into consideration the fact that the sphere gap voltage factors, milliampere readings, etc., are not sufficiently accurate by themselves, but that, in addition, the direct output of radiant energy should also be checked. Ionization methods, controlled by known and definite amounts of radium or other supplementary methods or system of measurements, should be employed as a check so that the quantitative tissue absorption can at least be approximately measured.

The water-cooled tube demands still greater accuracy as to dosages, and added precautionary measures must necessarily be instituted because of the greater volume of X-ray energy employed within a shorter period of time.

In conclusion, therefore, I wish to emphasize the very important essential requisite of correct dosage readings of quantity and quality in both our animal and human experimentations and practical X-ray and radium treatments, and the probable influence of even slight variations in dosage upon the phenomena of normal or abnormal tissue growths.

Benign giant-cell tumors of long bones.—A benign giant-cell tumor of the long bones, with characteristic clinical, macroscopic and microscopic findings, has long been recognized by surgeons and pathologists. The tumor usually grows slowly and produces little clinical evidence until it is large enough to cause pressure symptoms. The microscopic appearance of the tumor suggests an inflammatory origin. Trauma in the presence of focal infection may be the cause. Continued use of the term "sarcoma" in referring to this tumor is misleading, and unnecessarily alarms the patient. A sharp line of differentiation of benign and malignant types is advisable. The roentgen-ray findings, although of great importance as diagnostic and surgical aids, are not always characteristic. The treatment should be conservative. Curettage, followed by phenol, zinc chlorid, or the use of the actual cautery, is advisable. The prognosis in these cases is good as regards life, and good functional results in the extremities may be obtained unless the destruction of bone has been too extensive. Malignancy has been observed by Coley, Stone and Ewing in tumors that were supposedly benign. In the series of twenty-four consecutive cases seen at the Mayo Clinic between 1909 and 1922, in which operation was performed and microscopic examination made, twenty-three patients have been traced, from two to fifteen years after operation, and are without evidence of metastasis. The patients had been aware of the tumors on an average of twenty months before they presented themselves for treatment. The history and the clinical, laboratory, roentgenologic, macroscopic and microscopic findings should be considered in making a diagnosis, although experienced clinicians, surgeons, roentgenologists and pathologists may often diagnose these tumors correctly from the clinical or laboratory findings alone.

W. W. Wasson, M.D.

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RADIO-ACTIVE SUBSTANCES AND THEIR THERAPEUTIC USES AND APPLICATIONS

THE APPLICATION OF RADIUM TO VARIOUS TYPES OF TUMOR

By JOSEPH MUIR, M.D., New York

IT is now the consensus of opinion among radiotherapists that lymphoid tumors offer the conditions best adapted to treatment by radium or its emanation. Lymphosarcoma, however, though peculiarly susceptible to exposure to radium, is of such a malignant character, and so prone to metastasis, that few "cures" by the use of radium have ever been reported. Yet, as surgery, under these conditions, is even less effectual, radium still offers the greatest hope of amelioration, for, as it has been aptly phrased, the effect of radium is to strengthen Nature's barrier of lymphocytic infiltration, instead of sweeping it away by excision. Under radium therapy many of these sarcomatous growths have shown marked regression, and in certain cases, where the growth was still in its early stage when it first came under treatment, being still completely localized, the disease has apparently disappeared permanently. Though these instances are lamentably few, one has but to consider the practically universal recurrence of sarcoma after surgical extirpation, to realize that radium is offering a more cheerful prognosis than has ever before been held out to the unfortunates who become victims of this highly fatal malady. Sarcomata belonging to other groups, such as neuro- or osteosarcoma, have, however, proved uniformly resistent to any form of radiation.

Embryonal tumors of the testicle, which are highly malignant and peculiarly likely to metastasize, have been demonstrated to be exceedingly susceptible to radium, but, as with sarcomata, their tendency toward early metastasis makes any form of treatment of little avail unless the patient comes under the care of the radiologist very soon after the malignant process is initiated. Metastasis by the way of the venous system quickly gives rise to secondary tumors in widely separated parts of the body, such as the lungs, liver, kidney, stomach, or even the brain, and these very often so quickly attain large dimensions as to attract more attention than the original growth in the testicle. Many factors operate to make the diagnosis of these testicular growths obscure. They are often confused with syphilitic lesions, and frequently so much time is lost in the unavailing administration of anti-luetic treatment, that when the patient is finally placed in the hands of the radiologist, he is beyond the help of radium or any other therapy.

Yet, in those cases where treatment has been promptly instituted, the combination of surgery and radium exposure has given most encouraging results. Radium emanation enclosed in a 2 mm. lead filter has been successfully applied preliminary to operation, the usual dosage being twelve thousand millicurie hours at a 6 cm. distance. This same dosage is applied directly over the testicle as well as along the spermatic cord. In general, these growths have their original focus in the testicle proper, progressing thence to the epididymis, primary tumor of the epididymis being exceedingly rare, or, in the opinion of some authorities, altogether non-existent. The effect which radium has upon these tumors depends largely upon the type of cell which predominates in their structure. If adult tissue is largely present, the growth will prove much more resistent than in a case in which embryonal cells, in a state of rapid proliferation, are in the ascendancy.

Neoplasms of the vulva and vagina, which are most frequently of the epidermoid type, have given most encouraging results from treatment by buried radium emanation. In this particular application

of radium therapy it was found, as has already been mentioned in another connection, that tubes containing from 2 to 5 millicuries caused extensive necrosis about each area of implantation, and that the insertion of a greater number of tubes and their more extensive distribution, made the employment of smaller units of radium emanation—never more than 0.4 mc. and often no larger than 0.1 mc.—productive of far more satisfactory results. At present these minute capillary tubes are inserted directly into the malignant tissue by means of an instrument specially devised for this purpose, and, while exerting radio-activity sufficient to have a lethal effect upon the cancer cells, this activity steadily declines, for, as we have already shown, the radium emanation decays continuously at a rate which can be exactly estimated in advance. As the entire amount of the dosage which may be obtained from a "seed" containing any known quantity of radium emanation may be quickly reckoned by multiplying this quantity by 132, we are at once placed in possession of the information that the total dosage we may expect from, for example, a tube holding 2 millicuries of radium emanation, would be equal to that which we could secure from a tube containing 2 milligrams of radium element during 132 hours, or 264 millicurie hours. It must be remembered, however, that the radium element does not diminish in quantity, and thus remains constant in intensity, whereas the intensity of the radium emanation steadily diminishes.

Cancer of the vulva has responded well to the application of embedded "seeds" of radium emanation. In this type of lesion there is early metastasis to the lymph nodes of the groin, and any treatment of the original lesion will be doomed to failure unless this focus of metastasis is carefully considered and treated. Owing to the danger of disseminating the malignant cells by even the slight trauma incident to implantation of the capillary tubes, it is now generally considered expedient to first expose the primary lesion to filtered radium element, the same method being employed in dealing with the probable site of metastasis in the groin. Thereafter capillary tubes containing not more than 0.5 millicurie are implanted directly in the growth. The number of tubes employed is, of course, governed by the extent of the primary lesion when it comes under treatment. The tubes should be placed in the neighborhood of three-quarters of a centimeter apart, and in large growths inserted about the edge, still maintaining about the same distance between them. The exact condition of the inguinal nodes must be ascertained and "seed" implantation be carried out there, also, if it seems desirable, as it is in most cases. Usually the glands are first dissected out, after which capillary tubes are implanted at the femoral ring and also in the lymph nodes above Poupart's ligament. These tubes usually contain from 0.3 to 0.5 millicurie of radium emanation each, and are placed approximately one centimeter apart. Care must be used to avoid letting the tubes come in direct contact with blood vessels, for this may lead to serious or even fatal secondary hemorrhage. If the original focus is situated high up in the vulva, it is not unlikely that the glands upon both sides will be involved, and the technic thereby proportionately complicated, with increased likelihood of failure.

The use of radium in any form has until very recently been regarded by most workers in this field as being wholly inapplicable to cancer of the vulva. Our experience, however, has been quite otherwise, and the good results which have followed the use of emanation tubes buried directly in the growth, hold out most encouraging prospects for greater usefulness in the future. While the action of the embedded radium emanation may in some degree resemble that produced by cauterization, it differs from it markedly in that the gradual decline in activity and the steady lessening of the intensity of the radium emanation, while producing a reactive inflammation, is prolonged and gradual, so that often the lesion may be entirely eliminated without necrosis

or wide tissue destruction, and without the suffering incident to any of the cauterization treatments. If too large a dosage of the radium emanation is administered the evil effects just mentioned may follow its use also, but by keeping the radium emanation in each individual tube down to a very minute amount, never varying much from the 0.5 millicurie dose, the necrotic zone will be kept within its minimal limit, and practically no sloughing will follow the treatment.

Effective radiation of all the cancer cells of a given lesion will be difficult, if not impossible, if reliance is placed wholly upon the capillary tube method. While in very small growths this may be possible, in practice it has been found necessary to reinforce the "seeds" within the neoplastic tissue by an application of radium emanation to the surface above the growth. A similar application should be made over the inguinal glands, usually on both sides, as in cancer of the vulva, especially, these are likely to be bilaterally infected. The usual dosage employed is from one to two hundred millicuries of radium emanation, filtered by two millimeters of lead or of brass and a half millimeter of silver, the usual length of application being 350 millicurie hours. For vaginal lesions the "bomb" designed for the Memorial Hospital is an efficient means of application. This applicator is so made as to afford protection from the rays for the rectum and bladder, but permits a surface dosage for the lesion of a thousand millicuries of radium emanation filtered through one millimeter of platinum. This is customarily applied for an hour directly over the lesion. The same care in examination of the lymph nodes in the groin should be exercised with vaginal growths as was outlined for those originating at the vulva. As a routine, the external application, which can often be held in place by dental compound as has been done with such signal success in oral lesions, should be carried out in the same manner, to avoid metastasis to the groin from any form of malignancy of the external genitalia in either sex.

Location of "seeds" in vaginal carcinoma.—When the growth is situated in the lower third of the vagina some operators use additional radiation in the form of platinum tubes of radium element which can be kept in any desired position by means of dental compound. For lesions higher up this additional radiation can be given by using the "bomb," about one thousand millicurie hours being the average dosage. Growths on the anterior vaginal wall can be palpated through the rectum, which makes it easier to embed the capillary tubes of radium emanation satisfactorily. In general, the use of radium emanation has given better results than the filtered element, the effect of minute dosage evenly distributed appearing to be better than larger amounts of unvarying intensity concentrated at one limited point.

Mammary carcinoma.—In no form of malignancy has the use of unfiltered radium emanation, applied by the "seed" method, proved more successful and satisfactory than in the treatment of inoperable carcinoma of the breast. This particular lesion was one of the earliest to which the buried radium emanation tube was applied, but extensive experience among a considerable number of investigators has led to some modifications in the original form of application.

The capillary tubes are introduced directly into the lesion in the mammary tissue by means of the special instrument already mentioned, small quantities of radium emanation being employed—usually not over 0.5 millicurie to a tube—and the entire dosage designed to equal one millicurie of radium emanation to each cubic centimeter of tumor tissue. Gauging the dosage, therefore, requires measurement of the amount of malignant tissue which must be dealt with, and the accuracy with which this is accomplished has an important bearing on the efficacy of the treatment. A radiologist of sufficient skill and experience can usually estimate the amount of involved tissue so exactly as to make it possible to apply the entire dosage required at a single sit-

ting, providing always that there is no involvement of the axillary nodes. The implantation of the "seeds" should be made with judgment, particular care being exercised to avoid placing any of the tubes in direct contact with a rib or costal cartilage, as injury to the periosteum is a very serious complication. The tubes are implanted in the same manner as has been described for growths in the tissues of the external genitalia, the distance between them averaging about one centimeter.

Radiation of the axillary lymph nodes is more difficult to accomplish satisfactorily by the buried emanation method, and the whole problem of adequate treatment of malignancy in this situation is still far from being solved. In making implantations in the axillary region great care must be taken to leave an adequate distance between all the tubes and the tracts from the brachial nerve plexus, as in some earlier cases treated by this method most severe neuritis resulted from failure to observe this precaution. As we have experienced so much difficulty in making satisfactory implantations directly in the infected nodes, we have lately been following the technic suggested by Lee, which consists in placing 0.3 or 0.4 millicurie tubes of radium emanation about a half-centimeter apart along the course of the pectoral muscle, on its inferior posterior aspect. It is doubtful if the radiation effected in this way is adequate, but until our technic improves sufficiently to enable us to deal with the axillary region more satisfactorily, it appears to offer the best chances of success.

Operable breast carcinoma is still largely treated by excision, with subsequent prophylactic radiation, administered in the hope of destroying any malignant cells which may have escaped the knife. Roentgen-ray treatment is more generally popular for this purpose at present than is radium, but there is evidence that the employment of radium—especially the use of the buried radium emanation tube—is steadily gaining in favor in the handling of all types of malignancy and it is probable that the improvements and refinements in technic which are constantly being made, will still further extend its field of usefulness.

Recurrent carcinoma of the breast is peculiarly well suited to radium treatment, though the inevitably high mortality which attends this form of malignancy has so far obscured the actual accomplishments in this field. Enough, however, has been done to give assurance that lesions in the infraclavicular region, perhaps the most frequent location of recurrence, if they are not of great extent and are well localized, will prove amenable to applications of radium element, or its emanation applied in the form of a "pack." In skin metastases also, as well as recurrent carcinomatous areas which involve the thoracic wall, filtered radium emanation has done good service, in a number of instances causing a complete disappearance of the secondary growth, the patients remaining well for a considerable period thereafter. The use of radium in such cases is still of too recent occurrence to allow definite conclusions to be drawn, as in no case has a five-year period had time to elapse, but it can at least be affirmed that the outlook is encouraging in cases which have always heretofore been regarded as absolutely hopeless.

Practical application of biological effects.—This is a résumé, for the benefit of the general medical man, of the work which has been done and reported to special societies, on the biological effects of X-rays on tissue cells and new-growths. The practical application of these facts and principles to the treatment of lesions is developed, with the conclusion that in short wave length therapy we have a valuable agent for the successful treatment of many kinds of malignancy.

W. W. WATKINS, M.D.

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DEPARTMENT OF RADIODONTIA

UNDER THE SUPERVISION OF BOYD S. GARDNER, D.D.S.,
ROCHESTER, MINNESOTA

ADAMANTINE TUMORS OF THE JAW

WITH REPORT OF EIGHT CASES

By BERNARD F. SCHREINER, M.D., F.A.C.S., and WALTER L. MATTICK, M.D.
State Institute for the Study of Malignant Disease, Buffalo, N. Y.; Burton T. Simpson, M.D., Director

EIGHT cases of adamantinoma have been admitted to the New York State Institute for the Study of Malignant Disease. During this period, a total of 4,360 tumor cases of all descriptions were accepted for treatment, thus making the ratio of adamantine tumors approximately 1 to 545, or about one-fifth of 1 per cent of all tumors seen at this Institute. Although this type of tumor is not rare, it seems justifiable to report the following cases.

CASE 1. No. 5,499, admitted October 29, 1917, male, married, 38 years of age. Family history unimportant.

In 1913, the patient first noticed a soreness in the right lower jaw. He had a tooth extracted, believing this would put an end to the trouble. The soreness continued and, in 1916, he had three more teeth removed. At the time of admission there was a large lump in the lower jaw, but no history of "lumps" in the neck. Expectoration was excessive and there was a slight odor. The patient did not complain of pain.

Examination disclosed a well-nourished man, physically normal with the exception of the condition in the right lower jaw. The lower right first molar, both premolar and canine teeth were missing. Filling these cavities was a mass of what appeared to be granulation tissue. This discharged a slightly purulent secretion and bled easily. The jaw bone was thickened and the mucous membrane of the mouth was retracted over the growth. There was no metastatic involvement. The Wassermann was negative. *Clinical diagnosis:* Epulis. *Pathological diagnosis:* Adamantine epithelioma.

X-ray plate showed rarefaction of jaw bone from the incisor to the last molar in the lower right jaw, which extended over nearly the whole width of the bone.

On November 1, 1917, under ether, morphine and hyoscine, the tumor mass was scraped out and one incisor and molar removed. The tumor was soft, friable and gritty in places, and a brownish colored serum escaped. After removal of the tumor, the floor of the cavity was smooth throughout. This was left to granulate. At present the case is clinically well.

CASE 2. No. 5,534, admitted February 19, 1918, male, single, age 14 years. Family history unimportant. In July, 1917, he noticed a small swelling in the right lower jaw, which became sore when eating. He had had a decayed tooth in this sore area. This had been removed three months previous to admission. The swelling increased in size following extraction of the tooth.

Under ether anesthesia, incision was made along the lower border of the right jaw and several large hyperplastic lymph nodes, together with an immensely enlarged submaxillary gland, were removed. The mucous membrane of the mouth overlying the tumor mass, which involved the ramus and angle of the jaw, was then incised for a distance of 5 cm. and all the diseased tissue was curetted away with a sharp spoon. The cavity was then packed with gauze.

On April 19, 1918, X-ray treatment was begun, consisting of the following factors: 90 K.V., 5 ma., 7 min., 1.4. Al. filter, 21 cm. S.T.D. This was repeated every three or four weeks for nineteen treatments. On April 19, 1920, 50 mgs. of radium, con-

tained in a 1 mm. brass capsule with 1 mm. lead, was placed in the mouth for two hours. When seen in May, 1922, there was a palpable lymph node above the larynx which was freely movable, and one in the right submaxillary region. The swelling over the

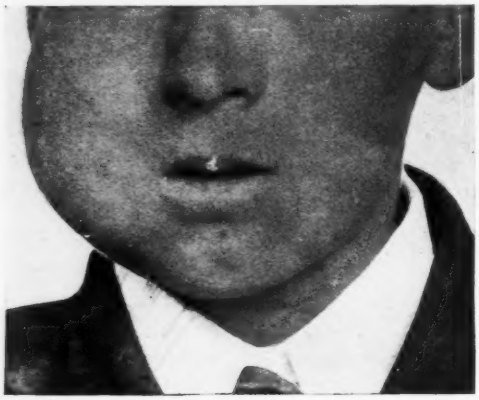

Fig. 1. Case 2. Boy aged 14 years, with adamantinoma of lower jaw.

angle of the right jaw was of a stony hardness, and the bony shell of the right jaw was irregular in outline.

In June, 1922, the tumor mass in the right lower jaw was growing. Later, seeds to the value of 799.68 mc. hours were planted into the growth and deep X-ray given. When last seen, the tumor mass was larger and there was ulceration in the anterior surface of the tumor.

Case 3. No. 5,777, admitted February 28, 1919, female, single, 12 years of age. Family history unimportant. She had previously had a swelling in the left lower jaw but this had disappeared after a few weeks. It appeared again about a week before admission and had increased noticeably in size. On examination she complained of difficulty in opening her mouth and of slight pain.

Physical examination was negative except for the inability to open her mouth widely because of the tumor mass which involved the left lower jaw in the region of the molar teeth. This extended posteriorly to the angle. The tumor mass was firm and showed involvement of the submaxillary region. *Clinical diagnosis:* Adamantinoma. Patient did not return for treatment.

Case 4. No. 6,612, admitted February 24, 1921, widow, housewife, 52 years of age. Family history unimportant. The patient noticed a mass in the left lower jaw in 1911 which did not bother her until three years previous to admission, when her throat began to get sore and the tumor increased in size. A year previous to admission she had an abscess in the left lower jaw and after that the mass grew larger and extended to the left side of the neck. The patient complained of much pain.

Examination was negative except for the lower jaw in the region of the molar teeth, where there was a diffuse tumor mass which was ulcerating at one small point near the angle of the jaw. At the base of the anterior pillar some granulation-like tissue protruded. The inner surface of the jaw bone over the tumor mass was thin and spongy. Peritonsillar and submaxillary nodes were markedly enlarged. The Wassermann reaction was negative. *Pathological diagnosis:* Adamantinoma.

An application of 8,412 mc. hours of emanation in a pack, screened with 6 cm. of cotton, 1 mm. of lead, 1 mm. of Al., and 0.5 mm. of silver, was made to the left jaw and four days later the tumor tissue was scraped out. Seven months later there was still an enlargement at the angle of the jaw and the bone was extremely thin. A radium pack was applied for a total of 5,888 mc. hours over the left submaxillary region. Six weeks later there was still thickening in the region of the lower jaw and in the floor of the mouth. There was no pain, neither were there palpable nodes in the cervical or peritonsillar regions.

On palpation, the jaw bone was hard and firm. Three more radium treatments were given and when the patient was last seen there was decided improvement. A small, slightly movable mass still persisted on the jaw bone.

Case 5. No. 6,700, admitted March 11, 1921, single, Indian, male, 25 years of

age. Family history unimportant. The patient had a chancre in 1919. His present illness was attributed to a fall downstairs, at which time some teeth were knocked out. Three years before admission he noticed a small growth on the inside of the left upper lip and face, which had gradually grown larger. The lip appeared swollen and pale. He was free from pain except when he had a cold. In the Summer of 1920 the patient had had four X-ray treatments which did not seem to reduce the size of the growth.

Fig. 2, Case 6. Appearance of jaw April 19, 1920, before treatment.

Physical examination was negative except for a large tumor mass in the region of the left bicuspid and the first molar of the upper jaw. This mass was of a bony or calcareous consistency. The mucous membrane was retracted over the tumor mass, which presented a ragged appearance. With a hemostat, the whole calcareous tumor mass was enucleated. On palpating the hard palate in this region the bone was found to have been pushed out of its normal position and presented a hard ridge inside the line of the teeth. There was evidence of old X-ray reaction in the upper lip. The skin was parchment-like. There were no palpable nodes in the neck. The Wassermann reaction was one plus. *Pathological diagnosis:* Adamantinoma.

Radium was applied in the cavity from which the tumor had been removed for 128 mc. hours, filtered through 0.5 mm. of silver and 1 mm. of brass. A month and a half later the lesion had healed and four months later the patient was discharged clinically well. To date there has been no recurrence.

Fig. 3, Case 6. Lateral view, April 19, 1920, before treatment.

CASE 6. No. 6,814, male, 4 years of age, native of the United States. Family history unimportant. He developed a small growth in the upper gum at the age of 7 months, at the time he was cutting his teeth. About a year before admission the child was seen at the State Institute for the Study of Malignant Disease. At that time the growth was more pronounced on the right side, but has since extended across the midline in the region of incisor teeth, to the left side. He had five X-ray treatments

by another physician when he was one year of age, but has had none since.

Examination was generally negative except for a slightly fluctuating tumor mass in the left upper jaw in the region of incisor

Fig. 4. Case 6. Appearance of jaw September 12, 1921, after treatment.

and bicuspid teeth, which caused a protrusion of the upper lip. There were no palpable nodes. The diagnosis made from tissue removed was adamantinoma.

He was operated upon under ether anesthesia. Two encapsulated tumors which apparently occluded both antra were removed. Fourteen days later 212 mc. hours of radium emanation was applied to the interior of the left antrum. A few months later there was no evidence of recurrence and the child was considered clinically well.

Case 7. No. 7,892, admitted February 21, 1923, married, male, 50 years of age. Family history unimportant. A few months before admission he had "neuralgia" in the lower right jaw and went to the dentist and had his teeth extracted. His jaw became swollen and he experienced considerable pain. A mass developed in the right lower jaw which made it impossible for him to eat other than soft or fluid foods.

Physical examination was negative except for a hard mass which occupied the entire right submaxillary region and jaw bone. The mucous membrane over it was smooth and not ulcerated. It gave "crackling" sensation to the touch. Wassermann was negative. The pathologist reported inability to find any enameloblasts and that the tumor gave the impression of being an epithelioma, although he could not definitely exclude adamantinoma.

The day after admission 1,600 mc. hours radium pack was applied over the right submaxillary region. A month later the right jaw was smaller but an inflammatory swelling had developed in the submental region, pressure on which caused pus to appear in the floor of the mouth. There were marked metastases in the right submaxillary and submental regions. The patient failed to return for further treatment.

Case 8. No. 8,690, admitted September 5, 1924, married, female, 28 years of age. Family history unimportant. She complained of a swelling in the left side of the chin which started about a year previous to admission and had gradually increased in size. Two molars in the left lower jaw were removed and since then the swelling had increased in size. She had no pain or discharge, but a feeling of discomfort and numbness. She had had no treatment, except local applications of iodine. At the time of her admission the lower left jaw was swollen. There was a tumor mass felt below the gum which apparently was in the medullary cavity of the jaw bone. There were capped teeth, and a bridge over this area. A clinical diagnosis of adamantinoma was made.

X-ray plate showed rarefaction of the bone at the site of the swelling on the lower left jaw. On September 18, 1924, under gas anesthesia, the capped teeth and bridge

were removed from the lower left jaw. The bicuspid and lateral incisor were also removed, and the gum was incised. Granulation-like tissue was exposed which had eroded the medulla of the jaw bone. The cavity was rough in areas. All tumor-like tissue and rough areas of bone were removed with a curette and rongeur forceps. The cavity was packed with gauze and two days later a tube containing 188 mc. of radium filtered through brass 2 mm., and rubber was applied for a total of 377 mc. hours. On November 21, 1924, the cavity in the left lower jaw bone was clean and healthy looking. There was a sequestrum removed on December 19, 1924, at which time there was no evidence of tumor tissue seen.

in the oldest (Table I). The average observed by Lewis is given as thirty-three years. Five occurred in males and three in females.

Esch, in 1921, reported a case involving the left upper jaw which for some time was diagnosed as a sinusitis with polypi formation. In 1919, Weichselbaum was able to collect from the German literature but five cases occurring in the upper jaw.

As the name signifies, this tumor arises from the adamantine cells of the enamel organ. Figure 5 shows a diagrammatic sketch of such organ, taken from Stöhr-Lewis, depicting its origin from the enamel organ or its remnants. Detailed description of the pathology can be found in Ewing's "Neoplastic Diseases" and will not

TABLE I.—ADAMANTINE EPITHELIOMA

Case No.	Date of admission	Age	Sex	Blood Wass.	Pathologic tissue rept.	Duration	Previous treatment	Location	S. I. M. D. treatment	Results
5,499	10-29-17	38	M	Neg.	Adamantine epithelioma	4 yrs.	None	Lower jaw	Oper. 11-1-17	Clin. well 2-8-18
5,534	2-19-18	14	M	3 + 2-18-18 Neg. 10-20-18	Adamantine epithelioma	7 mos.	None	Lower jaw	Oper. 2-21-18 1 radium 2-24-18 *small X* 1 radium 2 H. X-ray	Clin. well June, 1920 Recurrence, Jan., 1922
5,777	2-28-19	12	F	Neg.	Clin. diag. only. Biopsy refused	4 mos.	None	Lower jaw	Not treated	Failed to return for treatment
6,612	2-24-21	52	F	Neg.	Adamantinoma	8 yrs.	None	Lower jaw	4 radium	Temporary improvement
6,700	3-11-21	25	M	1 +	Adamantinoma	3 yrs.	4 X-ray 1 yr. ago	Upper jaw	Oper. 3-11-21 Radium 3-15-21	Clin. well, April, 1921. Did not return
6,814	4-25-21	4	M	Neg.	Adamantinoma	3½ yrs.	5 X-ray when 1 yr. old	Upper jaw	Oper. 4-26-21 Radium 5-10-21	Clin. well, 5-25-21
7,892	2-21-23	50	M	Neg.	Adamantinoma	2 mos.	Poultices	Lower jaw	Radium 2-22-23	Unimproved, Sept., 1923
8,690	9-5-24	28	F	Neg.	Adamantinoma	1 yr.	None	Lower jaw	Oper. 9-16-24 Radium 9-18-24	Clin. well, Dec., 1924

COMMENTS

Of these eight cases, six involved the lower jaw and two the upper jaw. The age of the first appearance ranged from four years in the youngest case to fifty-two years

be reviewed here. Krompecher does not consider these tumors uniform either as to histogenesis or morphology and states that he believes some may be derived from squamous epithelium of the mouth. Most

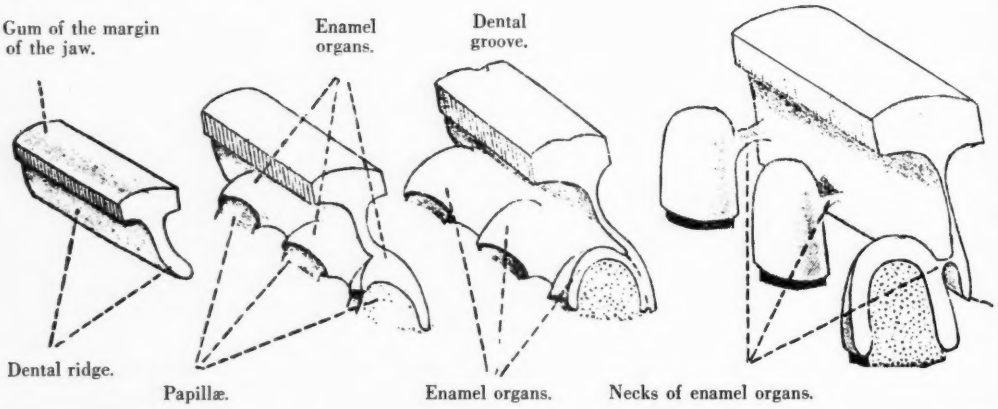

Fig. 5. Diagrams showing the early development of three teeth, one of which is shown in vertical section. (From Stöhr-Lewis' Histology, P. Blakiston's Son & Co., Philadelphia, 1906.)

authorities seem to consider finding stellar shaped epithelial cells very characteristic.

Adamantinomas arise from paradental epithelial debris and usually make their appearance in adult life. They are reported as occurring from the sixth to the seventieth year. One of our cases was in a boy of four years. Women are said to be more predisposed than men. The tumors occur in either jaw, more frequently the lower, and may be either cystic or solid. The former are said to be more common in the lower jaw, while the latter are noted as occurring more frequently in the superior maxilla.

These tumors occur near the angle of the lower jaw and often follow upon the extraction of teeth. The cystic tumors may be unilocular or multilocular. Albarran observed one that had been growing for thirty-eight years. The smaller tumors are generally easy to remove, while the larger ones prove more difficult. Although these tumors rarely metastasize, they do infiltrate and thus tend to recur after removal. The recurring tumor apparently takes on more malignant characteristics, thus giving rise to an unfavorable prognosis.

Ewing observed a "fibro-epithelial" tumor in this region which gave rise to metastasis of one of the cervical lymph nodes and also a nodule in the lung.

SUMMARY

1. Eight cases of adamantinoma are reported, six involving the lower and two the upper jaw.

2. These cases were treated by radiation therapy, either high power X-ray or radium, or by operation when it seemed advisable.

3. Of these eight cases, four remained clinically well, one recurred after being well for one and a half years, one showed temporary improvement, one was unimproved, and one failed to return for further treatment.

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CASE REPORTS AND NEW DEVICES

UNDER-EXPOSURE AS A DIAGNOSTIC POINT IN CASES OF NON-OPAQUE FOREIGN BODIES IN THE BRONCHI

By SAMUEL W. DONALDSON, A.B., M.D.,
St. Joseph's Mercy Hospital, ANN ARBOR, MICH.

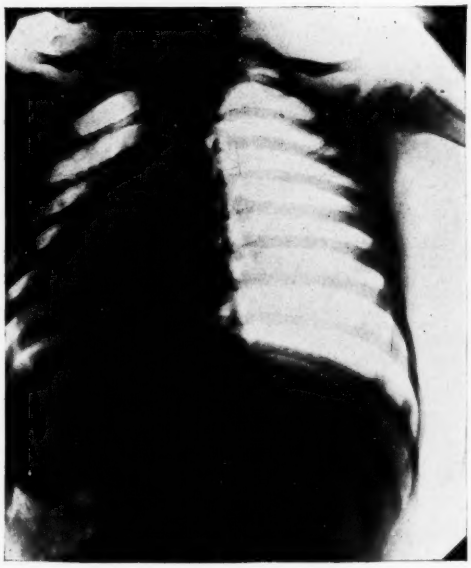
Radiographic examination of the chest in cases known to have or suspected of having a non-opaque foreign body in the bronchus is essential to demonstrate whether or not the following diagnostic points are present:

1. Increased radiability denoting emphysema on the affected side.
2. Decreased excursion and flattened diaphragm on the affected side.
3. Displaced heart and mediastinal structures toward the unaffected side.

These findings have been carefully treated by Drs. Manges and Jackson in medical literature, and, either singly or combined, considered to be of extreme importance. However, the films of some cases proven by bronchoscopy to have had such an obstruction do not show these findings with striking contrast, especially the emphysematous condition. Films showing this to a slight degree, but not enough to produce the other conditions, are viewed with a certain reservation by the surgeon, and the roentgenologist cannot definitely state that there is sufficient evidence present on which to base a positive diagnosis.

It has been the procedure in this laboratory to make additional films, other than those where the usual technic was used. This second set of films are carefully underexposed but fully developed.

Where there is only slight emphysema present the evidence is convincing. Insufficient penetration shows the unaffected side without any detail whatever, while on the affected side the increased air content of the lung allows the penetration used to give about the same detail one would expect to



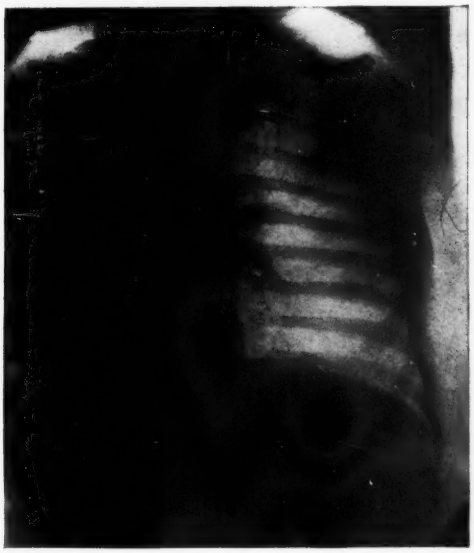
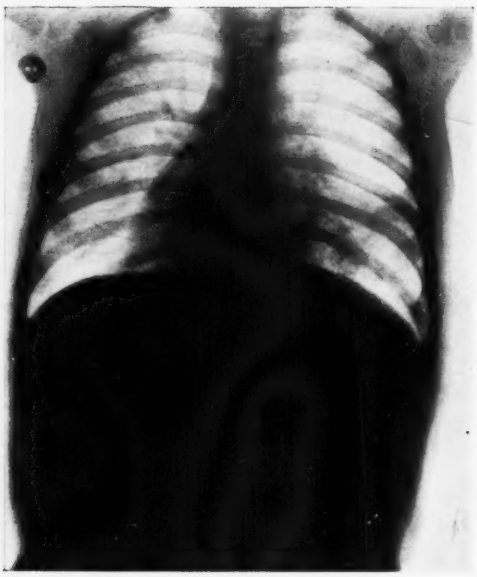


Fig. 1. (*a*) Fully exposed film showing the classical positive findings. (*b*) Under-exposed film of same case demonstrating the exaggerated contrast of the two sides. At operation a portion of a peanut was removed from the right primary bronchus.



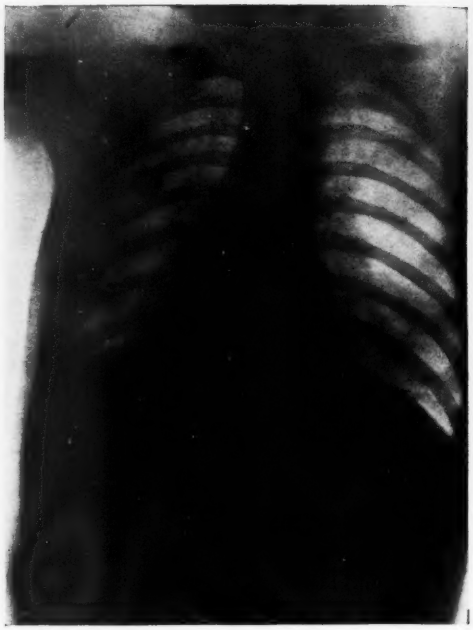


Fig 2. (*a*) Fully exposed film shows evidence of some emphysema in the upper right lung field and a small pneumonic area in the base on the same side. (*b*) Under-exposed film of same case. The increased radiability of the right side is more definitely apparent than in fully exposed film. At operation a peanut which had been aspirated by this child five days previously was removed from the right bronchus.

find in a normal lung field. This alteration in technic intensifies the contrast which might otherwise escape discovery.

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APPENDICEAL STONES SIMULATING GALLSTONES AND KIDNEY STONES

By SIMON ALBERT, M.D., PROVIDENCE, RHODE ISLAND

We have heard, perhaps too often, of appendiceal concretions being mistaken for ureteral calculi, or *vice versa*. Reports of such cases appear in the literature from time to time. It is unusual, however, to find a case where the appendiceal concretions have led to a diagnosis of kidney stones or gall-bladder stones. In view of this, the following case is reported. It is, in addition, an apt illustration of some of the abuses of laboratory methods.

L. B., a carpenter, aged 43, came under observation for non-radiating pain in the right upper quadrant of the abdomen, present at very frequent intervals over a period of slightly more than one year. The pain was described as "moderate" and "stinging" in character, increased by exertion such as his carpentry work, and relieved with fair promptness by rest. The pains were usually accompanied by chilly sensations. There had never been any really acute or prostrating attacks. There had been no jaundice. He complained of chronic obstinate constipation. Careful questioning revealed no other genito-urinary or gastro-intestinal symptoms. The physical examination was essentially negative except for very slight tenderness on deep palpation in the right upper quadrant just below the costal margin.

Fig. 1. Stones in upper right quadrant resembling gall-stones.

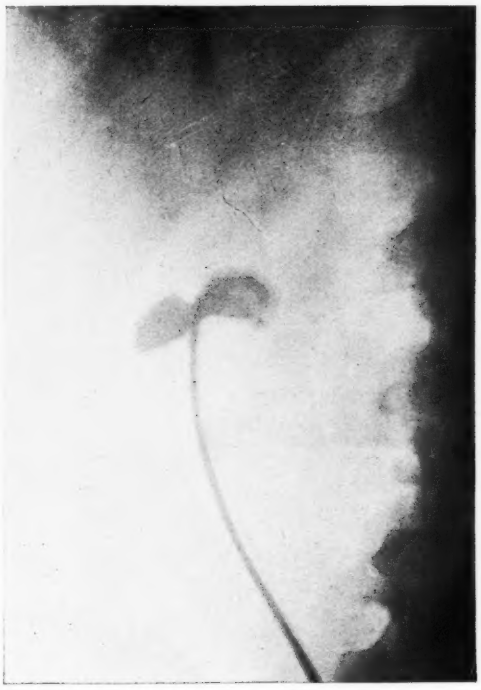

Fig. 2 Shows stones in close relation to ureteral catheter and overlying region of right kidney.

X-ray examination of the gall-bladder region was requested. This showed four well-defined calculi present at the level of the inferior surface of the liver, and near its outer margin. The X-ray Department reported that from the position of these calculi they appeared to be outside the gall-bladder region as well as outside the kidney region.

With this preliminary X-ray work, the patient was gone over very carefully by the G. U. service. They reported some tenderness to pressure over the region of the right kidney. On cystoscopy, the instrument passed easily into the bladder. The bladder urine contained a few flakes of macroscopic pus. The mucosa of the vault, fundus, and trigone showed a mild generalized cystitis. The catheter passed up the right kidney ureter 23 cm. and was thought to be not quite in the kidney pelvis. The patient stated that manipulation of the catheter in an attempt to "pass the obstruction" duplicated the pain that he complained of. The G. U. service reported "probable renal stone."

A barium meal was next given to study the relation of the stones to the duodenum. At this time, they were seen alongside the duodenal cap, in the usual gall-bladder position. No secondary evidences of gall-bladder disease were noted. The progress of the barium meal was not watched beyond the duodenum.

The kidneys also were radiated again with the opaque catheter in place, and were reported by the X-ray Department as showing no evidence of renal stone.

A pneumoperitoneum was then suggested by the medical service. This revealed the calculi, as previously reported, to be in close relation to the inferior surface of the liver, moving with the same on respiration. The X-ray Department changed its previous report and said that the evidence was very suggestive of biliary stones.

The medical service was firmly convinced that the patient had gallstones. The X-ray service was strongly inclined to agree with the medical service, although it was not quite satisfied. The G. U. service was so convinced of the stones being in the kidney

that they requested the patient be transferred for operation.

After prolonged investigation in the manner noted, the patient was turned over to the surgical service for gall-bladder operation. The usual right rectus gall-bladder incision was made. This was followed by a lower incision to get at the base of the appendix. The appendix was retro-cecal, running up along the ascending colon to above the kidney, just beneath the gall bladder. At this point, the appendix was kinked and the tip of it took a downward turn. There were many congenital bands running from the hepatic flexure of the colon and from the duodenum across and to the internal border of the liver and gall bladder. The appendix, containing four calcific fecoliths, was removed. The gall bladder seemed normal to the surgeon.

Fig. 3. Stones in tip of appendix (after removal).

The chief error, as far as the laboratory work was concerned, was the failure of the X-ray Department to carry out a more careful investigation, especially when they originally reported the stones as definitely outside both the kidney and gall-bladder regions. The clinical men were so insistent upon a gall-bladder diagnosis that they undoubtedly led the X-ray men into giving an unwarranted confirmation. It was a serious error for the X-ray Department to neglect to follow up the barium meal to its logical conclusions, namely a 6- and a 24-hour examination, even if they had originally reported gallstones. This might have saved them from the pitfall. It was a very reasonable thing to do under the circumstances and might have avoided an unnecessary ureteral catheterization, a pneumoperitoneum and other unpleasant sequelæ.

This leads to the following conclusions: (1) Radiographic shadows in the right upper quadrant may originate in viscera that normally occupy the right lower quadrant; (2) Clinically, right upper quadrant pain is not always gall-bladder or kidney pain, but may be appendix pain; (3) In all doubtful gall-bladder cases, a complete gastro-intestinal X-ray examination is highly desirable.

FIBROMYXOMA OF THE STOMACH PROJECTING INTO THE DUODENUM[1]

By THEODORE S. SWAN, M.D., Fellow in Medicine, The Mayo Foundation, ROCHESTER, MINNESOTA

In 1921 Carman reported the roentgenologic and pathologic findings in a case of hemangioma of the duodenum. Recently a case has been encountered with similar roentgenologic findings, due to a pedunculated tumor arising on the gastric side of the pylorus and projecting into the duodenum.

Case A469927. A man, aged forty-five years, came to the Mayo Clinic August 21, 1924, complaining of pain and tenderness in the precordial area, of three weeks' duration. The pain was brought on by exercise, was sharp, and accompanied by dyspnea and a choking sensation, with rapid irregular heart beats. The patient's appetite was good; he did not have indigestion. He had vomited occasionally, always without nausea.

The patient was a stocky, well built man, slightly anemic in appearance. His teeth

[1]Submitted for publication December 5, 1924.

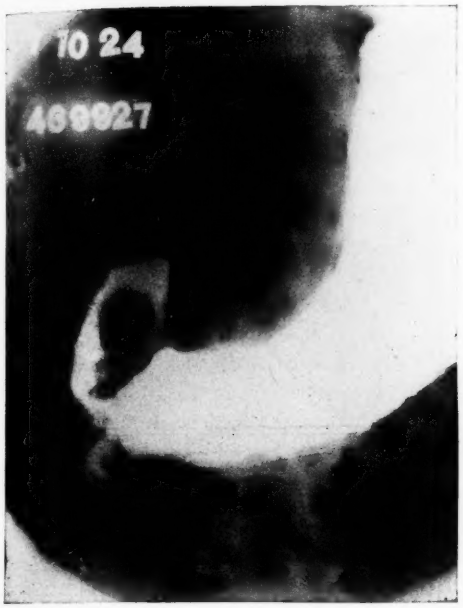

Fig. 1. A rounded, mottled filling defect in the center of the duodenum.

were in bad condition. He had moderate arteriosclerosis and slight cardiac hypertrophy. There was an aortic systolic murmur, and the blood pressure was 144 and 70; there was no edema. The prostate gland was moderately enlarged. Laboratory examination revealed a slight trace of albumin in the urine, secondary anemia with 3,270,000 erythrocytes, hemoglobin 47 per cent, color index of 0.7 per cent, and slight poikilocytosis, anisocytosis and polychromatophilia. Gastric analyses revealed achlorhydria, and total acidity 10. The stools were positive for occult blood. The electrocardiograph indicated a left ventricular preponderance. X-ray examination disclosed a peculiar deformity of the duodenal cap, probably due to a benign tumor, and on this basis an exploratory operation was advised, other supportive data being the secondary anemia, achlorhydria, and occult blood in the stools.

At operation a normal but distended pylorus, and a pedunculated gastric tumor attached to the upper wall of the stomach and extending 7.5 cm. into the duodenum were found. After placing a clamp on the pedicle at the level of the stomach, an incision was made 2.5 cm. above the pylorus on the greater curvature of the stomach, passing upward obliquely for 3.75 cm. toward the lesser curvature, and the tumor was removed through this incision. Removal of the tumor left a raw surface 2.5 cm. long, which was sutured over with chromic catgut. The pathologist's diagnosis was: Single ulcerated fibromyxomatous polyp (8 cm. long and 2 cm. in diameter).

Fig. 2. Single ulcerated fibromyxomatous polyp (8 cm. long and 2.5 cm. in diameter) attached at the pylorus and extending into the duodenum.

The character of the patient's symptoms did not suggest a gastric lesion; it was only revealed by X-ray examination which was made as a matter of routine.

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EDITORIAL

M. J. Hubeny, M.D. . . . . Editor
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DIRECT OR INDIRECT BIOLOGIC EFFECTS

The power of an idea is a marvelous thing. Even if the idea be wholly or partly false it is often astonishing how far it will travel before the truth can overtake and either destroy or correct it. When the true explanation of any scientific phenomenon is finally arrived at, its mechanism is generally found to be much simpler than most of the hypotheses previously held concerning it. The simple, the obvious, thing is generally the last to be thought of. Too often we forget that a hypothesis is nothing more than a plausible, but fanciful, explanation of certain observable phenomena, based partly on certain known facts, partly on circumstantial evidence and partly on the law of probability. Too often a quarter or a half truth is seized upon and by the generous admixture of an artificial mortar made up largely of wisps of imagination is erected into a figure supposedly representing the truth.

We have an example of this in the present attitude of radiologists toward the mechanism of the biologic effects produced by radiation. When living tissues are subjected to X-rays or to radium, certain changes follow. This we know, because it is a matter of daily observation. We know that such alterations occur in a fairly definite sequence. If we take the skin, for instance, we know that, according to the dose, the exposure will be followed by epilation, by erythema and atrophy, or by ulceration. No one would venture to attribute such effects to anything but reaction on the part of the tissues thus exposed to the rays. Yet, as soon as we approach the question of malignant disease, the notion is advanced by some that the biologic effect of the rays is due to the elaboration of protective substances leading to immunity. And this idea, once enounced, is copied and repeated until the utmost confusion reigns whenever the subject is brought up.

That the body attempts in various ways to neutralize or to limit the activity of malignant cells is undeniable. Evidence indicates that the blood and the tissue juices generally possess a definite lytic power against cancer cells, just as they do against bacteria. There is also substantial evidence that local defensive measures are instituted, but these must be subordinate to, and dependent on, the general defense mechanism. Among the local defense measures we may place: (1) the degree of differentiation of the neoplastic cells; (2) lymphocytic infiltration; (3) hyalinization; (4) fibrosis. The studies of Broders and MacCarty show that the degree of malignancy of a tumor depends on the proportional strength of each of these factors. Murphy and his co-workers have demonstrated that, under certain conditions, exposure to X-rays tends to intensify the lymphocytic factor of defense. *But this does not constitute immunity.* Proof that the systemic defense against cancer can be increased by radiations is still lacking. Indeed, all the positive information we have points to the conclusion that the cellular changes brought about by radiations in the case of malignant tumors are of the same order as those produced in normal cells; subject, of course, to the modifications imposed by differences in cell metabolism peculiar to the type of neoplastic process. Therefore, how can we write and speak of such biologic effects as being due to an immunity reaction?

On the contrary, a mass of evidence exists, all tending to show that the major factor in the effect of X or radium rays on cancer cells is a direct one. Mention has been made of the action of such rays on normal skin; it is impossible to see how such effects can be considered otherwise than as direct effects. In the experiments of Martin and Rogers, Dennis and Martin, and Warren and Whipple, in which destruction of the intestinal mucosa followed X-ray exposure under certain conditions, how can we interpret such results otherwise than as a direct effect? If this is true in the case of normal tissues, what basis have we for believing that diseased tissues behave differently? When connective tissue proliferation is found to have replaced masses of cells characteristic of some form of malignancy, why should we consider such proliferation due to indirect stimulation of connective tissue by the rays when pathology teaches us that such replacement is a universal tissue phenomenon following degenerative processes? Why invoke a mysterious, intangible mechanism, for which there is no adequate basis, when all available data, clinical and experimental, support the more simple view that radiation acts directly on the malignant cells, tending to destroy them or to interfere with their metabolism, and that their disintegration and subsequent replacement by connective tissue follows one of the main laws of general pathology? When we do so we place the cart before the horse, forgetting that the horse can make better progress with the cart behind rather than before him.

A. U. Desjardins, M.D.

AMERICAN HEART ASSOCIATION: ANNUAL MEETING

The first annual meeting of the American Heart Association was held at the New York Academy of Medicine, Monday afternoon, February 2, 1925. Dr. Lewis A. Conner, the President, reviewed briefly the progress of the development of the Association and commented on the need for such an organization and the widespread interest which its formation had developed. Dr. Haven Emerson, Chairman of the Committee on Membership, described the methods employed to reach all parts of the United States and Canada; regional agents covering one or more States have been appointed and already thirty-seven States are represented in the membership of the Association. The following program for the coming year was adopted:

1. *Maintenance of a Central Office.* As a headquarters through which all the work of the Association may be organized and directed. This office is already established, but the personnel must be increased to keep pace with the demands, which are increasing daily.

2. *Organization and Membership.* One of the first and most important steps in the development of the organization of the Association is that of securing contacts with all parts of the United States and Canada. This is to be accomplished by appointing regional representatives and obtaining a large and widely distributed membership.

3. *Educational Work.* Distribution of literature.—Publication of a monthly bulletin.—Lectures.—Loaning of charts and lantern slides.—Participation in public meetings of medical and health organizations.

4. *Field Work.* One or more workers with a knowledge of the most recent and approved methods for the prevention of heart disease and the organized care of cardiac patients, who shall be available to be sent to different sections of the country to encourage the establishment of new centers, demonstrate the methods found to be effective, and aid in solving local problems as they arise.

All present members of the Advisory Council were re-elected and the following were elected as new members of that body: Mr. Alfred Aiken, Dr. Linsly R. Williams, Dr. John Wyckoff, Dr. Robert Babcock, Dr. Joseph Miller, Dr. Henry Sewall, Dr. Emmet F. Horine, Dr. Frank N. Wilson,

Dr. Ross V. Patterson, Mr. William H. Hayes, Mr. Alfred B. Meacham, Mr. Herbert L. Kelly, Mr. Clayton M. Michael, Mrs. Fritz B. Talbot, Dr. Walter Wilson, Dr. S. A. Levine, Dr. Burton Hamilton and Dr. F. Janney Smith.

Those serving up to the time of the annual meeting as a temporary Board of Directors were re-elected as a permanent Board of Directors.

At the meeting of the Board of Directors immediately following the annual meeting, the following officers were elected: President, Dr. Lewis A. Conner; vice president, Dr. James D. Herrick; secretary, Dr. Robert H. Halsey; treasurer, Dr. Paul D. White; acting executive secretary, Miss M. L. Woughter, 1641, 370 Seventh Avenue, New York City.

HOW TO PREPARE AND TO DELIVER A PAPER TO A MEDICAL SOCIETY[1]

By E. S. MOORHEAD, M.B., B.Ch. (Dub.)
Associate Professor of Clinical Medicine, University of Manitoba, Winnipeg

Having listened for several years to the delivery of papers before this and other societies, I have from time to time tried to formulate a code of rules which would assist a member in preparing an address for an audience such as this. I have asked myself what makes the difference between a paper well prepared and well delivered, and another which, though given equal thought and care, has yet failed to interest the audience. Into the subject matter of a composition I will not enter. Each man, given a choice, will of course decide on a theme with which he is familiar, on which he has worked, and one which is likely to be of interest to those in front of him.

Many of the papers are designed with a dual purpose. First, for delivery by the spoken word, and, secondly, with a view to publication should the reception be favorable. Now, strange as it may seem, few papers prepared in a form adapted to publication are suitable for reading aloud. I will try to give you a reason for this. A published paper should, to be of value, have a bibliography with notes indicating the source and extent of information available to the writer. The reader of the journal, if he is interested, can identify the views of others quoted by the author. If, on the other hand, he wants to get to the subject matter, he can skip the bibliography, which is, after all, only an introduction. The paper that is read aloud may lose much of its value through too lengthy a reference to past writers, especially if it forms a preface.

For one thing, the audience has no way of verifying the quotations at first hand. Indeed, those who are going to take part in the discussion have probably looked up the authorities before coming to the meeting. In the second place, many members will become tired or bored trying to follow the reasons for a large number of loosely co-related statements or theories. Consequently, when the time comes for the speaker to give his own views, he finds that he has lost his grip on his audience. Some good lecturers quote authorities, as and when they need them, but they are sparing in their quotations, and they never wander very far from the subject matter. By all means, if you intend or hope to publish your paper, prepare a bibliography, but do not inflict it on your audience.

No speech and no paper was ever spoiled by being too short, but many have suffered from prolixity. My ideal is to leave my audience with a lingering regret that I had not gone on a little longer. Prepare your paper—prepare as long a paper as you like—and then revise it. Revise it with a blue pencil, and with two mottoes before you: "Brevity is the soul of wit" and "Precise knowledge puts an end to all conversation." When you have your paper at this stage, proceed to revise the English; see that your sentences run smoothly. If similar terms have to be used frequently, consult that

[1] Presidential address delivered before the Winnipeg Medical Society, May 16, 1924.
Reprinted by permission from the *Canadian Medical Association Journal*, December, 1924, p. 1202.

most valuable aid, Roget's "Thesaurus," in order that the same word may not be used time and again.

You must then read your paper aloud. Do it at home. Read it until your delivery is fluent. * * * Note whether you come within the time limit or not; if you exceed the limit, cut down. If a good speaker in a pulpit can in twenty minutes point out the way to eternal salvation, surely you can tell how to perform an operation or ameliorate a disease in a similar length of time.

Never apologize for your address, either at the beginning or at the end. To me, there is nothing more offensive than to be told by the speaker that he has hurriedly prepared his paper a short while before. If a group of intelligent and educated men pay you the compliment of coming to listen to you, the least that you can do is to offer the very best constructed material that is at your command, seeing that you volunteered for the work. If your paper is badly prepared, you insult your audience by telling them that you gave no time to it. If you say nothing in the way of apology, though they recognize that the paper is poor, they will give you credit for doing the best that you could, and your stock will be higher. Besides, your apologies may appear as a lame attempt to pay yourself a compliment. I have never yet heard a speaker at one of these meetings say that he had spent an immense amount of time in preparing and polishing his paper, and then apologize for it.

Do not make your paper so long that you have to race over it. Your audience wants to take breath just as much as you do. There is nothing more tiring than to have to listen to a paper delivered at high speed, and without time for rest or relaxation. If you want ideas to sink in, deliver them slowly and forcibly. You have two objects in preparing a paper: first, to propound some new method or idea; second, to elicit a healthy discussion. If the delivery is too rapid, members of your audience will not have time to formulate their views as you sweep them along, and though applause may be genuine, you will get neither criticism nor support.

Doctors are grave and dignified people, slow in thought and deliberate in action. They are not hustlers, and they do not like to be hustled. Besides, if your speed of delivery is rapid, you will not be able to take your eyes off the paper. If you cannot look up, then you cannot see how your paper is being received. It is always wise to have a few short-cuts marked in your paper; that is, places where you can leave out a paragraph or an example, without spoiling the sense. If on looking up on two or three occasions, you surprise several persons yawning, either behind their hands or openly, then you may be sure that the room is too hot or your paper too cold. If you find little groups of two or more in earnest conversation, then you have failed to secure their attention—the sooner you can bring your paper to a close the better.

Do not be hurt, because the fault is always with you. Your subject may have been too abstruse for tired men; your delivery may have been poor or monotonous; your paper too long. One thing you must remember: you set out to interest a group of men, and you failed to do so. Engrave that on the tablets of your memory, and do not overlook it when you prepare another address.

Do not stop a written paper to give verbal illustrations. If they are worth reporting, write them into the pages before you. In this manner you will not break the even delivery. It is a very difficult thing to come back to the written word, because you may have finished your illustration on the wrong note and in a halting style. It frequently looks as if you had been driven back to reading because the flow of your ideas had stopped. Besides, it uses up time which you had not included in your calculations. If you are at the beginning of the session it is selfish, and may spoil the later papers or discussions. If you are at the end, then the members are probably chafing to get away, and will give you scanty attention.

Finally, when your paper is ready, read a page of it, and then read a chapter of the

Bible. Ask yourself if your ideas are as clearly and tersely put as that best example of the English language.

CANADIAN RADIOLOGICAL SOCIETY

The sixth annual convention of the Canadian Radiological Society will be held this year from June 22nd to June 26th, in Regina, Sask., in conjunction with the Canadian Medical Association. Papers have been promised by the following guests and members: Dr. J. S. Pritchard, of Battle Creek Sanatorium, Michigan; Dr. G. E. Richards, of Toronto; Dr. A. J. Pacini, of Chicago, Illinois; Dr. A. H. Pirie, of Montreal; Dr. H. H. Cheney, of Montreal; Dr. D. A. Stewart and Dr. J. E. Pritchard, of Ninette, Manitoba; Dr. Mooney, of Edmonton, Alberta; Dr. W. H. McGuffin, of Calgary, Alberta; Dr. W. R. Gorrell, of Minnedosa, Manitoba; Dr. Frank Smith, of Winnipeg, Manitoba, and Dr. H. J. Ferrier, of Winnipeg, Manitoba.

The officers of the society, Dr. J. C. McMillan, Dr. W. H. McGuffin, Dr. G. H. Malcomson, Dr. C. M. Henry and Dr. E. C. Brooks, extend a cordial invitation to all members of the Radiological Society of North America to attend the convention.

Further details may be learned by communicating with the Secretary-Treasurer, Dr. E. C. Brooks, Royal Victoria Hospital, Montreal.

PROGRAM OF THE MID-ANNUAL MEETING

The papers to be presented at the Mid-annual Meeting of the Radiological Society of North America, to be held at Atlantic City, May 22-23, are as follows:

1. Radiation Treatment of Carcinoma of the Rectum, with Reports of 50 Cases. THOMAS JONES, M.D.
2. The Roentgen Treatment of Advanced Cancer. EUGENE T. LEDDY, M.D., Philadelphia.
3. Oral Administration of Tetra-iodo-phenolphthalein for Cholecystography. T. O. MENEES, M.D., and H. C. ROBINSON, M.D., Grand Rapids, Mich.
4. A Preliminary Report on the Jejunal and Oral Methods of Administering Tetra-iodo-phenolphthalein Sodium Salt in the Roentgenographic Visualization of the Gall Bladder. WILLIAM H. STEWART, M.D., New York.
5. Roentgen Diagnosis of Syphilis of the Stomach. LEON T. LEWALD, M.D., New York.
6. The Normal and Pathological Appendix and a Clinical and Roentgenological Study. ROBERT A. ARENS, M.D., and ARTHUR R. BLOOM, M.D., Chicago.
7. Stasis of the Ascending Colon Simulating Chronic Appendicitis. T. D. CUNNINGHAM, M.D., Denver, Colo.
8. The Rôle of Radiation in the Treatment of Cancer of the Breast. URSUS V. PORTMANN, M.D., Cleveland, Ohio.
9. Histologic Studies of Radiated Tissue in Cases of Carcinoma of the Breast. FRANK ADAIR, M.D., and EDWARD ELLIS, M.D., New York.
10. Report Covering Two Years' Experience with Deep Therapy in the Treatment of Malignancy. T. A. GROOVER, M.D., A. C. CHRISTIE, M.D., and E. A. MERRITT, M.D., Washington, D. C.
11. Practical *versus* Theoretical Application of High Voltage X-rays: Technic Learned and Results Being Obtained After Three Years' Observation. S. C. BARROW, M.D., Shreveport, La.
12. Obstruction of the Esophagus. J. D. OSMOND, M.D., Cleveland, Ohio.
13. Relative Indications for Surgical and Radiation Therapy in Certain Borderline Cases. IRVIN ABELL, M.D., Louisville, Ky.

14. Radium and X-rays in the Treatment of Round-cell Sarcoma: Based on a Study of 69 Cases. B. F. SCHREINER, M.D., Buffalo, N. Y.
15. Roentgenographic Examination of the Sphenoid Sinus. AMEDEE GRANGER, M.D., New Orleans, La.
16. Financing the Clinico-pathological and X-ray Laboratory in the Hospital, and also Conserving the Professional and Economic Interests of the Medical Personnel. BYRON C. DARLING, M.D., New York.
17. Roentgen-ray Study of 926 Cases of Rickets in Normal Children, in the District of Columbia. T. A. GROOVER, M.D., A. C. CHRISTIE, M.D., and E. A. MERRITT, M.D., Washington, D. C.
18. The Treatment of Carcinoma of the Fundus of the Uterus with Radium and Hysterectomy. LEDA JUNE STACY, M.D., Rochester, Minn.
19. Radiography of the Infant Chest, with Special Reference to the Progression of the Chest and the Determination of the Normal. W. W. WASSON, M.D., Denver, Colo.
20. The Laws of Development of X-ray Films. MR. R. B. WILSEY, Rochester, N. Y.
21. The Management of Toxic Goiter with Radium and Roentgen Ray; Results Controlled by Basal Metabolism. J. T. STEVENS, M.D., Montclair, N. J.
22. Hyperthyroidism. A. E. BARCLAY, M.D., Manchester, England.
23. A Practical Method for the Routine Determination of the Quantity and Quality of X-rays. EDWIN C. ERNST, M.D., St. Louis, Mo.
24. Metastasis to the Bones from Cancer of the Breast; A Roentgenologic Study. R. D. CARMAN, M.D., and H. W. MEYERDING, M.D., Rochester, Minn.
25. Compression Fractures of the Spine: Their Characteristics and Differential Diagnosis. L. R. SANTE, M.D., and LEX MCCUTCHEN, M.D., St. Louis, Mo.
26. Certain Difficult Problems in the Treatment of Carcinoma of the Lower Jaw. F. W. JOHNSON, M.D., Atlanta, Ga.
27. The Granulomata, Hodgkin's Disease, Lymphosarcoma, and Leukemia. ALBERT SOILAND, M.D., Los Angeles, Cal.

BOOK REVIEWS

THE PRINCIPLES AND PRACTICE OF ROENTGEN THERAPY. By I. Seth Hirsch, M.D., Director, X-ray Departments, Bellevue and Allied Hospitals, New York City. Diploma Radiology, Cambridge University, England. With Dosage Formulæ and Dosage Table by Guido Holzknecht, M.D., Professor of Roentgenology, University of Vienna, Director of the Central X-ray Department of the General Hospital, Vienna. With Three Hundred Illustrations and Fifty-seven Tables. American X-ray Publishing Company, New York, 1925.

Among those who study medical literature there is a constant argument regarding the relative values of journal literature and book editions. Undoubtedly the details of medical progress are printed in the journals. Book editions are the interval guideposts of medical science.

This elaborate book by Hirsch will serve as a record of the development of the science of deep roentgen therapy—as a textbook for students—as a basis of study for those who would know what they are doing and as a guide to the roentgen practitioner.

The schematic arrangement provides the natural division of the subject: Part I, The Generation of X-rays; Part II, The Measurement of X-rays; Part III, The Application and Dosage of X-rays.

The Dosage Formulæ and Dosage Table of Professor Guido Holzknecht of Vienna are elaborately displayed upon a large inserted schema, in addition to Holzknecht's alphabetical and classified disease indexes. This is a very important part of the book.

It is a most welcome addition to American and English X-ray literature. This is a most comprehensive outline and is worthy of intensive study by every roentgenotherapist. Possibly one may side-step the physics of deep therapy, but the practical outline of Holzknecht demands our attention.

Hirsch has disentangled, digested and then co-ordinated the theory and practice of deep therapy as reflected by the voluminous journal literature of America, England, France and Germany.

The reviewer is amazed at the comprehensiveness of contents within the limits of its pages. To illustrate this feature would demand the quotation of the content pages. Although warranted, it is impractical.

Delving into the book at different points lends satisfaction. The author constantly reserves a practical viewpoint in the midst of precision graphs and the almost mystical demands of the physicist. The deep therapy problem seems to be a conflict between the physician and the physicist at the best, with the poor patient occupying the proverbial lamentable position.

Only those who have followed roentgen literature carefully or those who have attempted with faltering steps to follow the leaders, can appreciate the labor, the drudgery and patience demanded of the author. Surely Dr. Hirsch will be rewarded by a wide distribution of the book. It is required by every student of deep therapy and should be available wherever deep therapy is practised.

X-RAYS AND X-RAY APPARATUS. An Elementary Course. By John K. Robertson, Associate Professor of Physics, Queen's University, Kingston, Canada. The Macmillan Company, New York, 1924. Price $3.50.

This is a real college text-book written for students of X-rays in the physics department of a university. After looking through the book one is attacked by the idea that it might be a good book for a physician who thinks he is a radiologist, because: (1) It presupposes very little knowledge of physics; (2) It is simply written for impressionable minds in the moulding, and (3) It is brief.

Do not be misled that the book is not comprehensive. It may start, and does, with the old illustration of the bar magnet and iron filings, but it rapidly progresses to Coolidge tubes, measurements of wave lengths, dosage of ionization and deep therapy. The simplicity of the author in his descriptions insures the integrity of his knowledge. No physician could be guilty of such splendid simplicity. The book is commended to all serious beginners—not technicians, and to the seasoned radiologist who may wish to find the complicated physical facts of X-rays, simply told. It is a real text-book.

NORMAL BONES AND JOINTS, ROENTGENOLOGICALLY CONSIDERED. Annals of Roentgenology, Volume IV. Two Hundred and Twenty Roentgen Ray Studies on Sixty-one Full-page Plates and Thirty-four Text Illustrations. By Isidore Cohn, M.D., F.A.C.S., Professor of Clinical Surgery, Tulane University, Associate Senior Surgeon, Touro Infirmary, New Orleans, La. With a Foreword by Rudolph Matas, M.D., Professor of General and Clinical Surgery, Tulane University, New Orleans, La. Paul B. Hoeber, Inc., New York, 1924. Price $10.00.

This beautiful volume is the fourth volume of the series of monographic atlases, known as the Annals of Roentgenology and edited by Dr. James T. Case.

The artistic book-making, exquisite Gowdy typography and excellent roentgen reproductions of the preceding volumes are continued. These features mark these Annals of Roentgenology as the most artistic publications in medical literature of the modern period. The publisher, Mr. Paul B. Hoeber, is to be congratulated upon his fidelity to an original idea and ideal.

The Foreword by Dr. Rudolph Matas is undoubtedly one of the most graceful and charming passages in medical literature.

As an encomium of Roentgen it has no equal. As an acknowledgment of the influence of roentgenology upon modern surgical diagnosis, it far exceeds the dreams of any roentgenologist. Coming from a master surgical clinician makes the message more pleasing. Although strictly scientific in its content, this Foreword of Matas exhibits the fluidity of Thoreau and the charm of Henry Van Dyke. You must read this.

Wherefore the book, which inspired such a glowing Foreword? It is a carefully planned study of normal joints at various ages. The shoulder, elbow, wrist, hip, knee and ankle are chaptered and each chapter has four divisions, to-wit: I. A review of the literature. In each instance this review will prove the justification for the present volume. II. Conclusions based on the study of the normal joints in question. III. Descriptive findings of individual roentgenograms of particular joints at various ages. IV. The importance to be attached to such a study from the surgical standpoint and suggestions of its value to others.

Cohn attempts to settle mooted points in epiphyseal development through the study of a large series of roentgenograms of certain joints. The elbow joint enjoys the greater portion of the book. Undoubtedly this is a reflection of Cohn's surgical interest in this particular joint. The management of fractures of the elbow and end-results are depicted in numerous illustrations and furnish much text. For the joints, other than the elbow, Cohn confines his illustrations and text to the normal development at various ages.

The book has no index. Perhaps this is unnecessary as one can turn to the particular joint and easily scan to certain desired information.

No other American roentgen atlas has approached the completeness of Cohn's meticulous studies and certainly such a volume is demanded in every roentgen laboratory. Possession of an authoritative atlas, such as Cohn's, with its analyses of conflicting epiphyseal differences, assures one of having a satisfactory reference volume. Its frequent usefulness will tax the binding.

We heartily commend Cohn's Atlas of Normal Bones and Joints to every careful roentgenologist and surgeon. And don't fail to enjoy the Foreword.

PIERRE CURIE. By Marie Curie. Translated by Charlotte and Vernon Kellogg. With an Introduction by Mrs. William Brown Meloney and Autobiographical Notes by Marie Curie. Illustrated. The Macmillan Company, New York, 1923. Price $2.25.

Sometime since this department reviewed the tribute to Pasteur by Duclaux, "The History of a Mind." This recorded the drama of Pasteur's laboratory life. There was little of romance in that life. The romance was in the influence of that mind (Pasteur's) upon civilization—the battle of the microscope with several national scourges and the conquest of them in turn. As yet there has been no Waterloo for the microscope.

This autobiographical volume by Madame Curie readily lends itself to contrast with the above. Marie Curie's tale is so simple. It is romantic. The lives of the Curies were so full of stress, strain and striving, so beset with disappointments and belated recognition and support; then the tragedy of Monsieur Curie's death by accident. All these miserable conflicts with life throughout the years and yet the saving romance of a great love, the simple romance of family life and children. The simplicity of these two personalities with a single scientific thought! It barely misses being sublime.

Sacha Guitry, the French actor-author, succeeded in writing and producing a drama entitled "Pasteur." It utilized the incidents of Pasteur's first dismal and unappreciated appearance before the French Academy of Physicians and his eventual triumph in later years as the dramatic peaks of the second and third acts. The play is bleak. There is no love in Pasteur's life to enliven the plot. It takes love to make the romance.

Pasteur can provide the drama—the psychological conflict of scientific jealousy.

How different the Curies! The romance of radium! The romance of these two scientists. And the pathos! It is quite true that this simple yarn of their lives as spun by Marie Curie does not record in words their pathetic devotion to science. But it is between all the lines.

The book was written by Madame Curie only after persistent solicitation and as a historical demand. Finally she consented. "But it will not be much of a book," she said. "It is such an uneventful, simple little story. I was born in Warsaw of a family of teachers. I married Pierre Curie and had two children. I have done my work in France." And again, "In science we should be interested in things, not persons." "I have tried faithfully to express the profound impression his p e r s o n a l i t y [M. Curie] made upon me during the years of our life together. I wish, too, that it might remind those who knew him of the reasons for which they loved him."

The devotion of Marie Curie to her scientist husband and lover is delicately portrayed in the biographical pages upon Pierre Curie. The simplicity of the scientist and mother is recorded in her brief autobiography. It seems almost as though such simplicity in the midst of the honors and gifts of the whole world was inspired.

Really, my dear reader, you cannot imagine a more romantic novel than this small volume. You could weep quietly with the sacrifices and denials of the heroine and you can glory in the scientific triumphs of the hero. Two scientists in love with their pursuit of the elusive metallic ray and in love with each other. Devoted to each other in science and in life and in death.

EDWARD H. SKINNER, M.D.

THE TREATMENT OF INFANTILE PARALYSIS. By Robert W. Lovett, M.D., Boston, Mass. Second Edition, pp. 175, 123 illustrations. P. Blakiston's Son & Company, 1012 Walnut St., Philadelphia, Pa.

This little book should be on the desk of every general practitioner, as well as specialist, for it is the physician in the outlying districts who sees the case of infantile paralysis in its early stages, and it is he who must guide the patient to as near a complete recovery as possible.

Infantile paralysis is becoming more prevalent each year, and the entire profession should give more study to this deforming malady.

The subject matter in this little work is well handled and profusely illustrated, and the bibliographical references given make this monograph complete and far-reaching in its methods. The pathology, symptomatology, and diagnosis are first taken up. The treatment is then followed through the three stages of the disease—the acute, convalescent and chronic. One entire chapter is given to the all-important subject of muscle training. The book is most complete in every phase, just such as might be expected from the pen of the late Dr. Lovett.

REX L. DIVELEY, M.D.

ABSTRACTS OF CURRENT LITERATURE

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The sella turcica.—In order to check the dimensions of the average normal sella, measurements were made on 500 normal roentgenograms. The minimal anteroposterior distance was 0.5 cm., and the maximal 1.6 cm. The depth varied between 0.4 cm. and 1.2 cm. The average anteroposterior distance was 1.06 cm., and the average depth 0.81 cm. The oval type of sella was found in 58 per cent, the round in 24.4 per cent and the flat in 17.2 per cent of the cases. Normal variations in the shape of the clinoid processes are not uncommon, and bony union between the anterior and posterior clinoid processes, producing a "bridged sella," exists in about 5.5 per cent of the cases. Such an anatomic variation seems to be of no clinical significance. The appearance of a "bridged sella" is frequently produced by faulty roentgen technic and localization which allows the images of the anterior and posterior clinoid processes to overlap.

From the roentgenologic standpoint, the pathologic conditions producing deformities of the sella are classified as follows:

1. Intrasellar tumors involving the pituitary: (*a*) primary, benign and malignant; (*b*) metastatic; (*c*) miscellaneous—gumma, tuberculosis and so forth.

2. Intracranial disease producing a chronic increase of intracranial pressure: (*a*) extrasellar tumors; hypophyseal duct, brain, those originating from the meninges, those originating from the bones of the skull, miscellaneous, such as abscess, aneurysm, and so forth; (*b*) hydrocephalus, congenital and acquired; (*c*) craniostenosis with oxycephaly.

3. Disease of the sphenoid bone: (*a*) primary, benign and malignant; (*b*) secondary,

invasion by malignant tumors of the nasopharynx, metastasis, multiple myeloma and fracture.

A tumor originating within the sella produces a deformity which is characterized by (1) uniform circular enlargement, (2) erosion and thinning of the dorsum sellæ, (3) blunting of the anterior clinoid processes, (4) erosion and distention of the floor, and (5) absence of intracranial pressure changes in other parts of the skull, except in advanced cases. In contradistinction to the characteristic deformity of intrasellar tumors, the pressure associated with extrasellar tumors produces a widened and flattened sella. As the pressure is transmitted from above, the posterior clinoids are eroded from above and become shortened and pointed. Varying degrees of destruction are produced, according to the duration of the pressure. The earliest roentgenographic evidence is a haziness or indistinctness of the floor, due to erosion and thinning of the bone. Hydrocephalus induced by causes other than cerebral neoplasm will produce changes in the sella exactly simulating those induced by extrasellar tumors.

Disease of the sphenoid will produce marked changes in the roentgenographic appearance of the sella. Changes secondary to a malignant tumor extending from the nasopharynx and invading the sphenoid are most common. With the exception of the dense shadows cast by osteomas or osteosarcomas, it is impossible to distinguish between the other tumors of either primary or secondary origin. In such conditions the sphenoidal sinus is increased in density or appears cloudy, there is a haziness of the floor of the sella, but, in general, unless the tumor has progressed to intracranial involvement, the contour of the sella is maintained and the contour of the clinoid processes may be distinguished.

J. D. Camp, M.D.

II. The Normal and Pathologic Anatomy of the Sella Turcica as Revealed by Roentgenograms. J. D. Camp. Am. Jour. Roentgenol. and Rad. Ther., Aug., 1924, p. 143.

Compton effect.—The authors discuss the possible influences of the Compton effect (change in the wave length of the scattered rays and emission of recoil electrons) on the biological action of the radiation used in deep therapy. The interesting discussions given, which unfortunately are not based on sufficient experimental evidence, come to the following conclusions: Since the true absorption would not be sufficient to account for the biological effect obtained, the Compton effect is also thought to be responsible for the biological action. The authors calculate that only about 6 per cent of the total radiation which enters the body (using 200 K.V.) can be expected to cause the biological effect: 2½ per cent of this is due to pure absorption and 3½ per cent to the absorption of Compton electrons. The authors conclude that an increase of voltage beyond that now used in deep therapy may be of advantage from the fact that when using increasing hardnesses and a scattering medium of low atomic number the emission of Compton electrons, compared to that of the photoelectrons, becomes more and more important.

Otto Glasser, Ph.D.

The Rôle of the Scattering on the Effect of Radiation, Taking into Consideration the Compton Effect. E. Lorenz and B. Rajewsky. Strahlentherapie, XVIII, 2, 1924, p. 473.

Radiation therapy in leukemia and lymphogranuloma.—The writers report the results of radiation therapy in 25 cases of leukemia and 46 cases of lymphogranuloma (Hodgkin's), treated at the State Institute at Buffalo. This method of treatment is still empirical, but tends to induce remissions with the least inconvenience to the patient. Medical treatment should be used in conjunction with radiation therapy. The use of this form of therapy resulted in temporary improvement in two acute cases. An optional dosage has as yet not been arrived at. Whereas very marked amelioration of symptoms and remissions followed such therapy, no permanent cures have resulted.

Solomon Fineman, M.D.

Results of Radiation Therapy in Leukemia and Lymphogranuloma. B. F. Schreiner and W. L. Mattick. Jour. Cancer Res., Dec., 1924, p. 504.

Indications for and results of injections into gasserian ganglion.—Injections of the gasserian ganglion are usually permanent, if enough alcohol is injected. At times one is able to inject the lower third or half of the ganglion and not involve the entire ganglion, but no one can promise this. Paralysis of the ocular muscles occurs at times, but always clears up. The absolute indication for injecting the ganglion is in carcinoma of the upper or lower jaw, or one side of the tongue. In outside injection as well as ganglionic injection, the prognosis can be made at the end of the month; *i.e.*, if anesthesia is present at the end of a month, it is apt to remain so. The results depend on just how much alcohol is distributed in the ganglion or posterior root, and, in the case of an outside injection, into the nerve fibers. Eye complica-

tions occur in about the same proportion as in division of the root by any other method. The writer has had no mortality.

W. W. WASSON, M.D.

Alcoholic Injections into the Gasserian Ganglion. George M. Dorrance. Jour. A. M. A., Nov. 22, 1924, p. 1678.

Gastric and duodenal ulcer.—It is the writer's opinion that there is no diagnostic history of ulcer, as was once believed and taught. The so-called ulcer history is only a hypersecretion history and may be produced by many other conditions besides ulcer. The physical examination of the patient affords no positive sign of ulcer, while negative signs neither indicate nor exclude it. In the examination of the stomach contents all the expected findings may be missing, even though an ulcer exists.

The roentgenologic examination is of the utmost importance, and no conclusion is justifiable without the evidence which this examination supplies. The roentgenologic examination supplies demonstration for inference and either confirms or disproves the suspicion aroused by other methods of investigation. However, X-ray reports are not infallible. An ulcer may be overlooked when present, or reported as present when in reality absent. It is the author's belief therefore that while X-ray findings are to be given great weight in diagnosis, they should be considered in connection with all other findings, elicited by history, physical examination, and other laboratory investigations.

SOLOMON FINEMAN, M.D.

Diagnosis and Treatment of Gastric and Duodenal Ulcer. W. F. Cheney. Calif. and West. Med., Dec., 1924, p. 595.

Radiation therapy of carcinoma of the cervix.—In regard to radiation therapy of carcinoma of the cervix, three points are emphasized in this study: radium and roentgen rays are of great value for checking the progress of disease and relieving the distressing symptoms of advanced cancer of the cervix. Patients with recurrent cancer of the cervix can be greatly benefited by ray therapy undertaken before the lesion is too extensive. Prompt post-operative irradiation is imperative, and to neglect it seems to be inexcusable.

The cases forming the basis of these premises are classified in accordance with the foregoing indications. The records extend over nine years, arranged in three periods of three years each. During the first period, from 1915 to 1917, the treatment consisted generally in repeated applications of small amounts of radium at the site of the lesion over several weeks, and various attempts at cross-fire through the rectum. In the next period, from 1918 to 1920, the principle of cross-firing the entire pelvic field was instituted. Radium capsules were inserted into the cervical and lower uterine canal in tandem arrangement and the so-called bomb applicator, holding a gram of radium, was inserted in the vaginal canal directed toward the right parametrium, the cervix, and the left parametrium, for 1,000 mc. hr. in each position. This internal application was supplemented by external application of radium in six positions about the pelvic girdle. Since the advent of the third period, from 1921 to 1923, roentgen rays have replaced radium for external irradiation. This combined treatment was completed in from seven to ten days. Primary cases received, on the average, 6,000 mc. hr. gamma irradiation in and about the cervix, and four roentgen exposures of 15 minutes each, with 5 mm. aluminum filter, 12 inch focal distance, 10 inch spark gap, 90–110 kilovolts, and 5 mm., through four fields converging toward the center of the pelvis, *i.e.*, right and left iliac areas anteriorly, and right and left sacral areas posteriorly.

In very stout patients with a heavy abdominal wall, external irradiation was usually omitted. In patients with elevated temperature and with evidence of local infection or pelvic cellulitis, treatment was delayed until the active inflammatory symptoms had subsided. Very advanced cases, with extensive involvement of surrounding structures, were not treated by irradiation, since this only adds to the pain and distress and tends to shorten life. Since very anemic patients fail to react favorably to radiation therapy —locally as well as constitutionally—an effort should be made to overcome the anemia by preliminary blood transfusion.

Primary Cervical Cancer.—Of 93 patients with primary cervical carcinoma—early, borderline and advanced—under treatment during the first period, only 4 are alive. In the second period, 266 patients with primary cervical cancer in various stages were treated, and 42 (15.8 per cent) have survived. There were 202 hopelessly advanced cases with 25 (12.3 per cent) survivals; 39 borderline cases with 8 (20 per cent) survivals, and 25 early cases with 9 (36 per cent) survivals. The results were obtained without primary mortality, but rectovaginal or vesicovaginal fistulas resulted occasionally at first from over-enthusiastic treatment of advanced cases. During the last period, 335 patients have been treated, of whom 169 (50.4 per cent) are alive.

Recurrent Cervical Cancer.—Of 53 patients treated in the first period, only one is alive, whereas 22 (19.1 per cent) of 115 patients treated in the second period have survived. In the

final period, 78 patients were under treatment and 42 (54 per cent) are alive. This class of patients was treated, when possible, with the vaginal bomb applicator, buried bare tubes and external irradiation. When shortness or stenosis of the vaginal canal rendered the lesion inaccessible and prevented the use of the bomb applicator the results were less satisfactory.

Irradiation after Hysterectomy.—Two patients treated in the first period have died. Of 22 patients observed during the second period, 14 (63.6 per cent) have survived without evident recurrence. All of the 7 patients treated in the final period are alive.

JOSEPH MUIR, M.D.

Cancer of the Uterine Cervix, Treated by Irradiation. Methods of Treatment and Results in 1,024 Cases. Harold Bailey and William P. Healy. Jour. A. M. A., Oct. 4, 1924, p. 1055.

A cancer-producing substance.—When isoprene $CH_2{:}C(CH_3)\cdot CH{:}CH_2$ is passed through a tube filled with hydrogen and heated to 820° C., a mixture of compounds, chiefly aromatic, is formed; this material produces cancer in mice more rapidly, and in a larger percentage of animals than do many samples of coal tar. This "isoprene tar" should provide a material for the study of cancer-production which is simpler than coal tar, for elements other than carbon and hydrogen can be present in it in traces only; whether the cancer-producing substance is composed of carbon and hydrogen only must remain uncertain.

W. W. WASSON, M.D.

The Formation of a Cancer-producing Substance from Isoprene (2-Methyl-Butadiene). E. L. Kennaway. Jour. Path. and Bacteriol. (Gt. Brit.), July, 1924, p. 233.

Radiation of glands.—The effects of radiation on glands may be inhibitory or destructive, and the hyperactive gland is more sensitive, so that it is logical to assume that the ductless glands when hyperactive will be more sensitive to the effects of radiation, and this assumption is confirmed by clinical experience.

The thymus gland is very easily affected, when hyperactive, by either X-rays or radium, and when diagnosis of this condition is established, radiation is indicated. However, diagnosis is not easy, as the gland may be hyperactive without being enlarged, and may be enlarged and still be perfectly normal.

In treating goiter by radiation, the matter of greatest importance is the proper selection of cases. There must be hyperthyroidism, and the early cases with soft thyroids react better than long-standing cases with hard glands. The early, distinctly toxic case is especially the one to be selected.

Exposure is made over three areas, two over the thyroid and one over the thymus, medium wave length and relatively short distance. No exposure should exceed two-thirds of an erythema dose and this should not be repeated within three weeks.

W. W. WATKINS, M.D.

Radiation Therapy of the Thyroid and Ductless Glands. George W. Holmes. Boston Med. and Surg. Jour., July 3, 1924, p. 10.

Cancer dosage.—X-ray treatment of the malignant uterus is usually confined to cervical cases, except where pre-operative or post-operative treatment is desired for fundus cases. Probably a combination of radium and X-ray is preferable in treating cancer of the cervix. Proper dosage is a much-discussed subject, some believing that the effect is direct on the cancer cell and therefore heavy dosage is required; others think the action is indirect from lymphocytic infiltration. The author's observation has been that the dose applied should be all that the normal tissues will stand without permanent injury, and should be given within a week's time from the start of treatment. Repetition of large doses is not borne well. It is not believed that radiation removes from the patient the conditions which brought about the cancer and, therefore, is not a cure for malignancy, even though the local lesion may disappear.

W. W. WATKINS, M.D.

X-ray Therapy—Carcinoma of the Uterus. Robert H. Milwee. Jour. Okla. St. Med. Assn., Aug., 1924, p. 201.

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